American Journal of Obstetrics and Gynecology

VOL. XXVII ST. LOUIS, JANUARY, 1934 NO. 1

Original Communications

RADIATION THERAPY IN CARCINOMA OF THE CORPUS UTERI*

WILLIAM P. HEALY, M.D., NEW YORK, N. Y.
(From the Memorial Hospital)

DESPITE the fact that hysterectomy is regarded as the treatment of choice for carcinoma of the corpus, many cases occur in which this procedure would be associated with grave risk of a fatal outcome because of other complicating conditions.

The greatest number of cases occur in the sixth decade of life, the average age in our series was 54.7 years.

Practically all of the patients therefore are beyond the time of the menopause, many are over sixty years of age, and it is to be expected that degenerative lesions such as those associated with advanced age, cardiac and renal disease, arteriosclerosis, diabetes, and obesity would occur rather often.

When such lesions do occur in association with carcinoma of the corpus, it is evident that a major surgical procedure, such as, hysterectomy should be avoided if possible.

For a long time it has been quite generally assumed that, since carcinoma of the corpus is a glandular variety of cancer, it is radiation resistant, and radiation therapy could, therefore, not be used to advantage to control the tumor growth.

However, radiation has been used in patients who declined operation or were poor risks for major surgery because of advanced age or other complications, and it has been noted that such patients were often benefited and indeed at times apparently cured by the treatment. Moreover

*Presented at the Fifty-Eighth Annual Meeting of the American Gynecological Society, Washington, D. C., May 8, 1933.

under the follow-up systems now in vogue in all first class hospitals, it was recognized that a great many of the patients in whom hysterectomy had been done did not remain well but developed local recurrences or distant metastases two or three years after operation and ultimately died of cancer. So that the conviction is gradually being forced upon us that hysterectomy does not give as satisfactory or permanent a cure as we believed.

Mahle[1] was one of the first to study a large series of surgically treated cases of corpus cancer from the histologic standpoint. He had no difficulty in dividing the cases into four different groups or grades according to variations in histologic structure and based upon MacCarthy's[2] standard of cellular differentiation.

Mahle's four grades and Ewing's[3] classification are quite similar representing a division into papillary adenoma malignum, adenoma malignum, adenocarcinoma, solid cellular or diffuse carcinoma.

Mahle especially recognized that a definite relationship existed between histologic structure and end-results in surgically treated cases as no deaths occurred in the most differentiated type Grade 1 in his series whereas in Grade IV, the least differentiated type, no case survived five years. He says "the postoperative prognosis of a group of patients with adenocarcinoma can be determined by a close study of the cellular differentiation of the carcinoma." Lindsay[4] and later Healy and Cutler[5] confirmed these results.

The histologic classification followed in the present report is similar to that used by Healy and Cutler[5] in a previous study of this subject.

Grade 1.—Papillary adenoma malignum, Fig. 1. The growth is entirely papillary and may not be superficial but as a rule does not tend to infiltrate the myometrium. It resembles adenomatoid endometritis and the cells show very little change from the normal.

TABLE I. TREATMENT OF PAPILLARY ADENOMA MALIGNUM, GRADE 1

	CASES	ALIVE	DEAD	AVERAGE AGE	AVERAGE DURATION OF LIFE	PER CENT ALIVE
Radiation alone	3	3	–	58.6 yr.	3.6 yr.	100
Radiation before hysterectomy	7	7	–	53.3 yr.	3.7 yr.	100
Radiation after hysterectomy	3	3	–	48.0 yr.	5.6 yr.	100
Radiation before and after hysterectomy	1	1	–	----	3.0 yr.	100
Hysterectomy	–	–	–	----	----	–
Total	14	14	–	----	----	100

There were 14 cases in this group. All of the patients are alive and well. Radiation alone was used in three cases. Each received an intrauterine application of radium with two or three capsules for from 3,000 to 4,000 millicurie hours with 0.5 mm. gold and 2 mm. black rubber filtration. Two of the patients also received a high voltage x-ray cycle of four exposures. They have remained well for two, four, and five years respectively.

Seven patients received intrauterine application of radium followed in from six to ten weeks by hysterectomy. The pathologist found evidence of persistent or active disease in only one uterus thus suggesting that radiation alone might have sufficed. These patients have survived one to twelve years. Three patients underwent hysterectomy followed by x-ray therapy, they have survived five, five, and seven years. One patient received x-ray and radium therapy before and after hysterectomy. She has remained free from evidence of disease for three years but has a vesicovaginal fistula.

From these results it would seem that we are justified in assuming that this histologic type of cancer of the corpus is curable in all cases by adequate radiation therapy or by hysterectomy.

Grade 2.—Adenoma malignum, Fig. 2. The microscopic picture is characterized by large or giant glands, often greatly elongated, lined

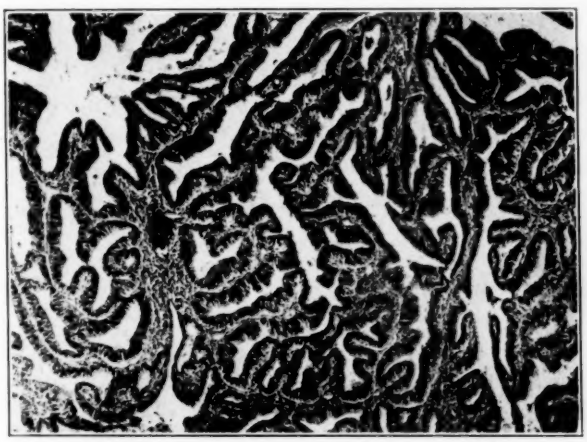


Fig. 1.—Papillary adenoma malignum, Grade 1.

by several layers of cuboidal and cylindrical cells. The stroma is greatly reduced and the enlarged glands adjoin each other, often in groups of three or four surrounded by strands of stroma. The nuclei of the gland cells are large and hyperchromatic and stain deeply. Any tendency on the part of the cells to break through into the stroma and to form solid masses takes the tumor out of this group and places it in the next one (adenocarcinoma).

This is our largest group, it contained 58 cases. The lesion is commonly found in association with fibromyoma and seems to be held in check by the myometrium for a long time before invasion of the uterine wall occurs and before extension beyond the uterus takes place. For this reason even though symptoms may have been present for two years or more and the patient may seem to be quite debilitated and the prognosis quite grave, a gratifying result may nevertheless be obtained with radiation therapy.

The treatment in 27 cases or nearly half the group was limited to radiation. This consisted of radium applied within the uterus in every case and in addition one or more x-ray cycles to the pelvic field unless the patient was obese. Seventy-four per cent of these cases treated only by radiation are alive and the average duration of life since treatment is 5.3 years. Patients who died were in an advanced stage of cancer when first seen or had serious medical complications and treatment was regarded only as palliative.

In this histologic group 21 other patients were given radiation with intrauterine radium alone or combined with x-ray and subsequently in six to ten weeks panhysterectomy by the abdominal route was done. It

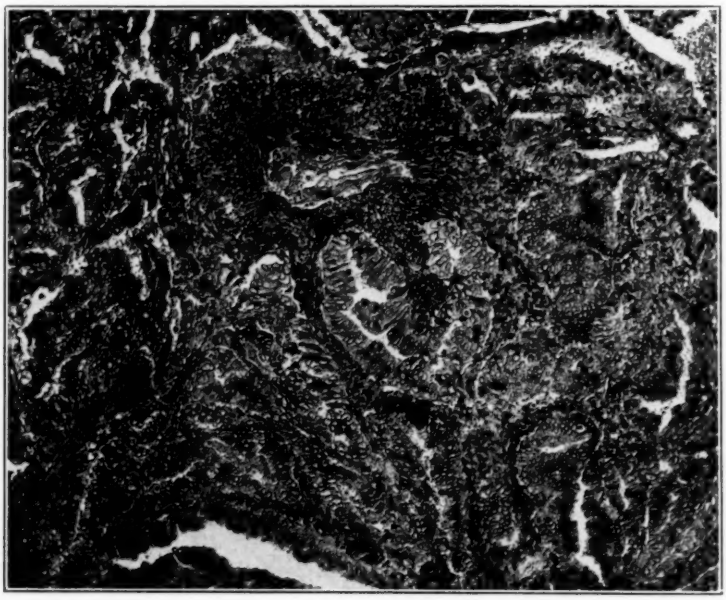


Fig. 2.—Adenoma malignum, Grade 2.

is of interest to note that the surgical procedure was on the whole little affected by the previous radiation. Ninety and one-half per cent of these cases treated by radiation first and hysterectomy later have survived for an average of five years.

Of the entire group of 58 cases of adenoma malignum, Grade 2, 84.5 per cent are living from one to fifteen years since treatment.

Grade 3.—Adenocarcinoma, Fig. 3. Histologically the cases in this group are characterized by greater malignancy. The cells are more atypical, there is more evidence of anaplasia than in the preceding groups and the tumor while still retaining its glandular arrangement, nevertheless infiltrates the stroma and forms solid masses of tumor cells. It is this evidence of infiltration which distinguishes Grade 3 from Grade

TABLE II. TREATMENT OF ADENOMA MALIGNUM, GRADE 2

	CASES	ALIVE	DEAD	AVERAGE AGE	AVERAGE DURATION OF LIFE		PER CENT ALIVE
					LIVING CASES	DEAD CASES	
Radiation alone	27	20	7	58.8 yr.	5.3 yr.	1.13 yr.	74
Radiation before hysterectomy	21	20	1	53 yr.	5 yr.	2 yr.	95
Radiation after hysterectomy	7	6	1	50 yr.	4.4 yr.	3 yr.	85.7
Radiation before and after hysterectomy	2	2	–	56 yr.	2.5 yr.	0 yr.	100
Hysterectomy	1	1	–	39 yr.	2.3 yr.	–	100
Total	58	49	9	-------	------	-------	84.5
Hysterectomy with or without radiation 31 cases, 2 deaths, 93.5 per cent living.							

TABLE III. TREATMENT OF ADENOCARCINOMA OF CORPUS, GRADE 3

	CASES	ALIVE	DEAD	AVERAGE AGE	AVERAGE DURATION OF LIFE		PER CENT ALIVE
					LIVING CASES	DEAD CASES	
Radiation alone	21	15	6	59.6 yr.	4 yr.	6 mo.	71.4
Radiation before hysterectomy	14	8	6	55.5 yr.	5 yr.	2.4 yr.	57
Radiation after hysterectomy	9	3	6	53.5 yr.	3.5 yr.	2.2 yr.	33.3
Radiation before and after hysterectomy	1	1	0	52 yr.	1.5 yr.	0	100
Hysterectomy alone	1	0	1	-------	------	2 mo.	0
Total	46	27	19	-------	------	------	58.7

2 and takes the tumor out of the adenoma malignum group even though the greater part of the histologic structure may resemble adenoma malignum.

Twenty-one patients in this group with adenocarcinoma, Grade 3, received only radiation therapy consisting of intrauterine application of radium and external application of x-ray to the entire pelvis. The average age of these patients treated by radiation only was 59.6 years. Fifteen of them are alive and well for an average of four years each. The 6 who died were treated for palliation only, as they all had metastases at the time treatment was started. The average duration of life in these fatal cases after treatment was six months. One patient seventy-six years old lived fourteen months, during which time the uterine

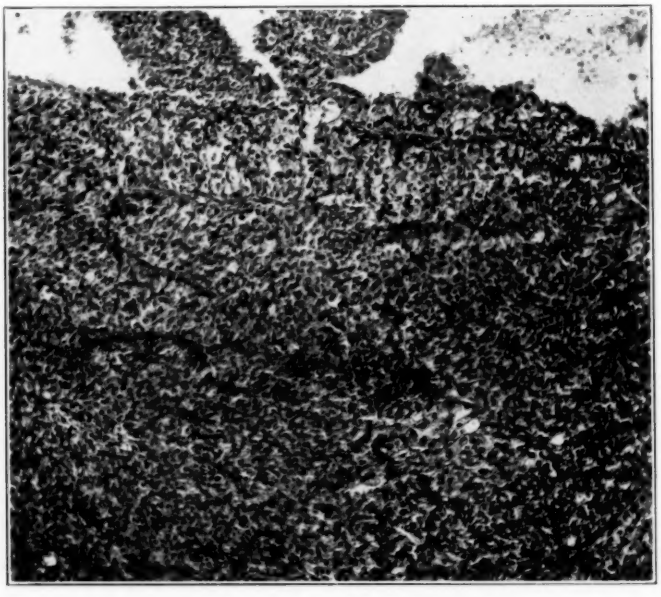


Fig. 3.—Adenocarcinoma, Grade 3.

bleeding and discharge and the pelvic discomfort were greatly diminished. Several of the patients were treated solely for relief of pain due to spinal or other bone metastases and with fair success.

In nearly every instance radiation was chosen as the method of therapy because the patient was advanced in years or in disease, and was for these or other reasons regarded as a poor risk for surgery.

In two of the cases a second diagnostic or control curettage was done about four months after the first curettage, no evidence of persistent or residual disease was found in either instance.

Although we have not done the second or so-called control curettage as a routine procedure in our cases, we are inclined to believe that it may be desirable to do so if one plans to restrict treatment to radiation. Burnam[6] recommends that it be done ten or twelve weeks following the

first treatment. This may be somewhat early depending upon whether or not one is also using external radiation.

Fourteen patients received radiation therapy before hysterectomy, and 57 per cent of these patients have remained well for an average of five years. It is interesting to compare this with the next group of 9 patients in whom hysterectomy preceded radiation, only 33.3 per cent of these patients are alive for an average of three and one-half years.

Even though the number of cases in each of these two subgroups is small, we believe the marked difference in end-results in favor of preoperative radiation is worthy of serious consideration. It would suggest that a much more favorable response to radiation may be expected when it is given in an adequate dosage as a preoperative measure.

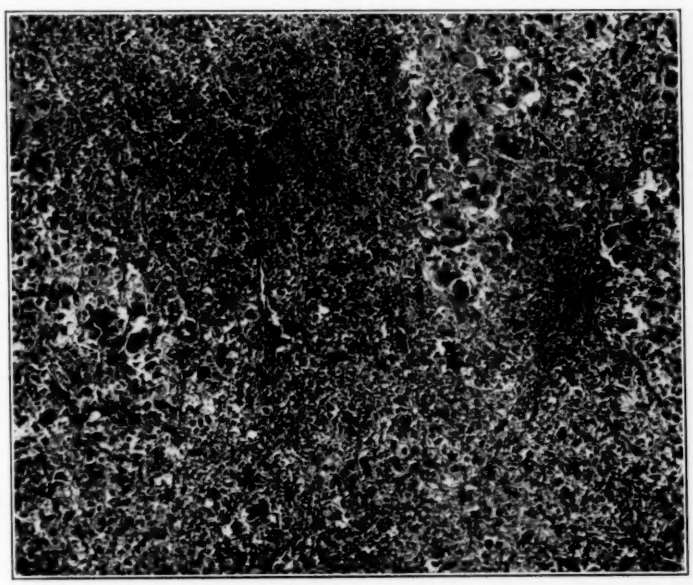


Fig. 4.—Cellular (anaplastic) adenocarcinoma, Grade 4.

It would seem to inhibit the growth capacity of the cancer tissues and diminish thereby the chance of metastases or local recurrence thus making the surgical procedure safer.

The increased malignant character of this histologic type of cancer cell is indicated clinically by the end-result for the entire group of 58.7 per cent as compared to 84.5 per cent for Grade 2 adenoma malignum.

One should also note that end-results obtained in patients with adenocarcinoma of the corpus treated by radiation alone, were superior to those resulting when hysterectomy was combined with radiation. In the former group 71.4 per cent of the patients are living whereas in the latter group only 50 per cent are alive.

It is interesting to observe that the end-results in the patients of this histologic type of corpus cancer treated by radiation alone are almost

identical with that obtained in the adenoma malignum Grade 2 group, 71.4 per cent in the former and 74 per cent in the latter.

It would seem reasonable to assume that radiation therapy is equally effective in controlling the disease in both histologic types. It must again be emphasized that the reason for limiting the treatment to radiation was in nearly every instance the patient's poor general condition which would entail too grave a risk if hysterectomy were done.

On the other hand there is a wide difference in end-results in both groups when hysterectomy is combined with radiation, 50 per cent in this group as against 90 per cent in the preceding group.

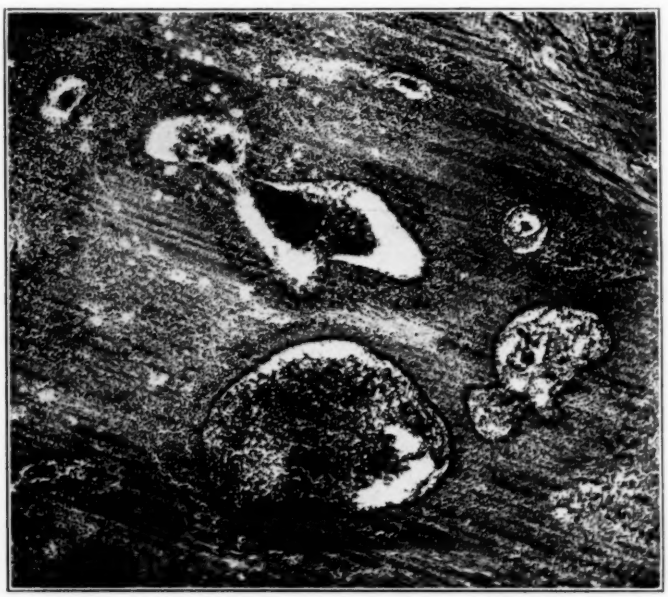


Fig. 5.—Diffuse anaplastic carcinoma, Grade 4. Persistent perivascular cells in necrosing carcinoma.

It would seem from these statistics that hysterectomy in patients with adenocarcinoma of the corpus tends to diminish the chance of permanent cure and to place a handicap on the patient.

Grade 4.—Cellular (anaplastic) adenocarcinoma, Fig. 4.

Cases in this group are characterized histologically by diffuse growth

TABLE IV. TREATMENT OF CELLULAR ANAPLASTIC ADENOCARCINOMA OF CORPUS UTERI, GRADE 4

	CASES	ALIVE	DEAD	AVERAGE AGE	AVERAGE DURATION OF LIFE	PER CENT ALIVE
Radiation alone	2	2	–	68 yr.	4.5 yr.	100
Radiation before hysterectomy	3	3	–	52 yr.	2.5 yr.	100
Radiation before and after hysterectomy	1	0	1	50 yr.	2 yr.	---
Radiation after hysterectomy	2	0	2	55 yr.	6 mo.	---
Total	8	5	3	56.25 yr.	------	62.5

of small round and polyhedral cells often entirely lacking in glandular arrangement. The cells may be closely packed together, stroma scanty. Mitotic figures numerous and marked evidence of anaplasia is seen.

There were 8 patients in this group. The significant fact would seem to be that despite the extremely malignant histologic characteristics of the lesion, the patients have done fairly well when radiation was resorted to as an important part of the treatment (Fig. 5).

Two patients, each sixty-eight years of age, each treated by two intrauterine applications of radium remain well and free of evidence of

Fig. 6.—Adenoacanthoma.

recurrence for two and seven years respectively. In each instance the uterus was extensively involved in disease, and operation was out of the question.

The three patients treated with radiation before hysterectomy are alive but one of them now has clinical and x-ray evidence of a chest metastasis one year after hysterectomy.

Adenoacanthoma, Fig. 6, a rather infrequent but distinct histologic variety of corpus cancer presenting a combination of glandular and squamous structure. Either variety may predominate over the other.

TABLE V. TREATMENT OF ADENOACANTHOMA OF CORPUS UTERI

	CASES	ALIVE	DEAD	AVERAGE AGE	AVERAGE DURATION OF LIFE	PER CENT ALIVE
Radiation alone	3	3	0	65.6 yr.	5 yr.	100
Radiation before hysterectomy	5	4	1	58.2 yr.	5 yr.	80
Total	8	7	1			87.5

There were 8 patients in this group. All are alive except one who died from an undetermined cause two months after hysterectomy. The patient was sixty-two years of age, and the uterus was removed some weeks after intrauterine application of radium. The study of the uterus revealed only radiation necrosis and no evidence of residual cancer.

In reviewing all the cases reported in this study, a total of 134, it is interesting to note that there was no mortality associated with either radiation therapy or hysterectomy. However, in one of the cases in the Grade 4 group of anaplastic adenocarcinoma which had been fully treated by radiation, we are of the opinion that the patient would have done better if hysterectomy had been omitted, as she was symptom-free at the time but soon developed evidence of extensive pelvic and retroperitoneal recurrence.

From the results of treatment shown in Tables I to V of this report, it is evident that the results represent different plans but always based upon radiation or hysterectomy, alone or in combination.

It is important to note that 100 per cent of all Grade 1 patients and 87.5 per cent of the Grade 2 patients are alive regardless of the plan of treatment followed. This would seem to indicate that the disease in these histologic types remains localized to the uterus for a long time, and if risk of hysterectomy is not unduly great, a cure may be obtained by this procedure. On the other hand when operation is contraindicated, radiation may be carried out to advantage.

Only 63 per cent of the patients with adenocarcinoma are alive. We would expect this histologic type of disease to be more malignant and to spread more rapidly to structures beyond or distant from the uterus, as it is an infiltrating disease which enters lymphatics as well as blood vessels.

CONCLUSIONS

I believe it is highly significant that the patients with adenocarcinoma of the corpus in which radiation was used in full dosage, either alone or some weeks before hysterectomy, have remained free from recurrent or metastatic disease and have lived longer than those patients with adenocarcinoma of the corpus treated by hysterectomy before radiation or hysterectomy alone.

In view of the marked difference in end-results in the two major histologic types represented by the adenoma malignum type of tumor and the adenocarcinoma type and, therefore, as emphasized by Mahle, the prognostic value of knowing as soon as possible in which histologic group the case falls, it would seem highly desirable to obtain, if possible, tissue from within the uterus for microscopic study before even the curettage is done. If this is not feasible, a quick report either from frozen section at the time of curettage or in four or five hours would be helpful in planning treatment.

In adenocarcinoma it is my impression that even with patients in whom conditions seem to be entirely satisfactory for hysterectomy, the

patient's interests will be best served by instituting full treatment with intrauterine application of radium and if feasible deep roentgen ray therapy previous to hysterectomy. Also in order to permit the full effect of radiation to be obtained the operation should be delayed 4 to 6 weeks following radiation. Postoperative radiation with radium applied in capsules throughout the length of the vaginal tube and an x-ray cycle should be utilized as an additional precautionary measure 8 to 12 weeks after the hysterectomy in cases of adenocarcinoma.

TECHNIC

Since practically all patients suffering from cancer of the corpus have passed the menopause, it would seem reasonable, when a patient at this age develops uterine bleeding and no other evident explanation is found for it, to assume that we may be dealing with endometrial cancer and to resort to one high voltage x-ray cycle before attempting diagnostic curettage. We have not, however, resorted to this plan as a routine.

In general our plan in all cases has been diagnostic curettage, at which time radium capsules are placed in the uterus end-to-end in sufficient number to cover the length of the uterine cavity from the internal os to the fundus. The filtration of these capsules is ½ mm., gold, covered with 2 mm. of black rubber, and they contain sufficient radon so that a total dosage of 3,000 to 4,000 millicurie hours will be given according to the length of the canal and the number of capsules in twenty-four to thirty hours. Usually the average dose is about 3,600 millicurie hours. We do not like to leave the applicator in the uterus longer than thirty hours, as we have a feeling that where long applications of 40 or more hours have been given within the corpus or the cervix, there has been more constitutional and local disturbance than in shorter applications. Within two or three days following the application of the radium, the x-ray cycle may be given. Hysterectomy, if planned, is not done for about six weeks. We believe it is important to again emphasize that with this plan there has been no operative mortality in this series of 134 cases and rarely any undue difficulty in the operations.

Our high voltage x-ray cycle has the following factors:

The pelvic girdle is divided in 4 quadrants, two anterior and two posterior. A treatment of 700 R units is given to each quadrant over a field 10 x 12 cm., 200 k.v., ½ mm. copper, 1 mm. aluminum filtration; 50 cm. target skin distance, 30 milliamperes current.

REFERENCES

(1) *Mahle, A. E.:* The Morphological Histology of Adenocarcinoma of the Body of the Uterus in Relation to Longevity, Surg. Gynec. Obst. 36: 385, 1923. (2) *MacCarthy, W. A.:* A Biological Conception of Neoplasia, Its Terminology and Clinical Significance, Am. J. M. Sc. 157: 657, 1919. (3) *Ewing, James:* Neoplastic Diseases, 1928, W. B. Saunders & Co. (4) *Lindsay, W. S.:* Variations in the Prognosis of Endometrial Carcinoma as Indicated by the Histological Structure, Surg. Gynec. Obst. 44: 646, 1927. (5) *Healy, William P., and Cutler, Max.:* Radiation and Surgical Treatment of Carcinoma of the Body of the Uterus, Am. J. Obst. & Gynec. 19: 457, 1930. (6) *Burnam, Curtis F.:* The Treatment of Cancer of the Body of the Uterus by Radiation, Ann. Surg. 93: 436, 1931.

FAILURES IN TUBAL STERILIZATION (MADLENER)*

A Clinical and Histologic Study

William H. Rubovits, M.D., and Alfred J. Kobak, M.S., M.D.,
Chicago, Ill.

(From the Departments of Obstetrics and Pathology of the Michael Reese Hospital and the Nelson Morris Institute, and the Department of Obstetrics and Gynecology, University of Illinois, College of Medicine)

A RELIABLE technic for tubal sterilization has been an objective for years. Many methods have been tried, but none have been able to stand the test of time. Some operations for tubal closure became almost universally popular, but the literature shows that invariably all methods are insecure because of isolated cases of subsequent failures. The late John Osborn Polak[1] made the following pertinent comment in his last annual review of the gynecologic literature: "Pregnancy has occurred after all methods of tubal sterilization. Hysterectomy and bilateral salpingo-oophorectomy are the only positive safeguards."

Many articles in the literature have dealt with the status of tubal sterilization and its failure. A review of some may be quite interesting. In 1897, Emil Ries[2] reported a study of the tubal stumps after salpingectomies. He showed where the ligated stumps reopened and advised that the interstitial portion of the tubes must also be excised to prevent a subsequent pregnancy. Experimentally, the study of tubal sterilization has been frequently associated with failures. Fraenkel[3] in 1899 condemned simple ligature when this method was successful in only two of thirty-three rabbits. Offergeld[4] studied simple crushing and ligature in rabbits, dogs, and cats, and this method also proved no safeguard against pregnancy. Leonard[5] in 1913 reviewed the subject and presented the difficulties in producing sterility by operations on the fallopian tubes. He cites cases of failure following ligature, wedge-shaped excision and burying the uterine end of the tubal stump, section of the tubes with cautery, removal of the interstitial portions, and also cases of bilateral salpingectomy.

Douglas,[6] Polak,[7] Zangemeister[8] and Burckhard[9] reported instances in which pregnancies followed salpingectomy. The latter two contributors cite interesting and similar cases in which the tubes were removed in the course of operations for successive ectopic pregnancies. This was followed by intrauterine pregnancies that were delivered at full term. They do not state how the interstitial portions of the tubes were treated. However, Lasch's case[10] of bilateral salpingectomy was definitely associated with a wedge-shaped removal of the interstitial portion of the tube, which was sewed over in two layers, but pregnancy followed at a later date. Liepmann[11] reported an abdominal pregnancy to follow a supravaginal hysterectomy.

Although ligation of the tubes and other sterilizing methods did not result in a permanent and complete interruption of the continuity of the lumen, histologic studies of such tubes are rather scarce. Kojima[12] studied the tubes that were suc-

*Read at a meeting of the Chicago Gynecological Society, May 19, 1933.

cessfully closed by the Madlener method. He found the lumen completely destroyed and the tube at the site of the operation replaced by fibrous and muscle tissue. Köhler[13] describes the histologic changes in unsuccessful closures by simple ligature. Nürnberg[14] shows that the ligature affects a local atrophy of the tubal muscularis; the muscle then retracts to both sides of the ligature, which then only encloses the mucosa and the serosa. This releases the constricting action about the lumen which becomes patent again. This author, and Kalliwoda[15] illustrated beautifully how a tuboperitoneal fistula formed at the site of the ligature, thus offering a new avenue for migration of the ovum into the uterus. Nürnberg's monograph in 1917, and Pokrowsky's[16] review in 1932 discussed the numerous tubal failures that may be found in the world's literature.

The Madlener technic[17] of surgical closure of the tube won many adherents. His original method was to raise a "knuckle" of the tube at its midportion. With the tube at an obtuse angle a broad area was crushed to paper thinness, and then the furrow of the crushed area was tied, which thus included two portions of the tube and a portion of the mesosalpinx. There have been minor variations in this technic but the essentials have been preserved. In 1926, he reported on 119 successful cases.[18] Wasser[19] had only one failure in 225 cases, and that one was an ectopic pregnancy. Baksecht,[20] of Leningrad, also reported this method to be satisfactory. However, more recently, many cases of failures have been reported.

Perhaps the best check on all forms of operative closure of the tubes is now available through the medium of lipiodol visualization. This method is simple, and localizes the tube where the operation failed. When the Madlener sterilizations are scrutinized postoperatively by this method, they show a much larger percentage of failures. Thus Fuchs and Lork,[21] studying 12 cases this way, found that only 7 had perfect results. In 2 cases there was an abdominal spill and in 3 the tube filled out up to the fimbriated end without a free spill into the abdominal cavity. Wolf[22] found that 8 of his 36 cases in which the Madlener closure was attempted were functional failures because the lipiodal passed the point of crushing and was visualized up to the fimbriated end. The lack of free spill of the lipiodol was explained as the result of a progressive endosalpingitis proceeding from the crushed area and secondarily closed the abdominal ostia of the tubes. In addition to the lipiodal studies demonstrating the failure of the operation other isolated reports have been noted recording failures of the operation, but we have not been able to find instances in which histologic studies have been made.

It is striking that the many ingenious methods devised for closure of the fallopian tubes meet with failures. Gynecologists are recognizing more and more that the fallopian tube possesses unusual regenerative powers. Hadden[23] reports 2 cases illustrating the rapidity of tubal regeneration. Rosenberger[24] reports the reopening of a closed tube when he relaparotomized his patient. Fuchs and Lork studied the tubes after crushing and ligation and found that this procedure did not destroy the tubal epithelium but merely gave rise to its shifting or displacement. The same authors describe an instance in which a subserous excision of

a certain length of the tube had regenerated completely. Serial sections failed to show the point of epithelial reunion and revealed only a slight atresia of the muscularis of the tube.

Sampson's[25] admirable study of postsalpingectomy endometriosis indicates very definitely how the tubal reunion may occur in certain instances. He regards the behavior of tubal epithelium in repair of salpingectomy wounds as a striking exception to the rule governing the healing of operative wounds of hollow viscera. In the stumps of tubes, sprouts of its epithelium often invade the wall and grow beyond it. It may continue to grow after the healing is complete. This phenomenon is designated by Sampson as endosalpingiosis. The incidence of endosalpingiosis was as great in stumps following tubal sterilization as in those following salpingectomy for salpingitis. "Postsalpingectomy endosalpingiosis usually arises from sprouts growing out from the traumatized mucosa of the tubal stump. These sprouts may invade not only the wall of the stump but also may extend beyond it, invading the tissue in which it is buried or any structure adherent to the stump." Sampson also stated that the misplaced tubal mucosa may assume the structure and function of uterine mucosa.

THE CLINICAL MATERIAL USED IN THIS STUDY

Madlener's method for tubal sterilization, which became quite popular during the past decade, has been used by one of us (W. H. R.) in 75 cases. This was the operation of choice because of its simplicity, its rapidity, and its freedom from loss of blood or from hematoma formation in cases of marked vascularity of the structures as one frequently notes during the performance of a cesarean section. We have observed 2 patients in whom a Madlener operation was performed and who subsequently became pregnant. Segments of the tubes were removed in order to determine by histologic study the reason of the failures of this operation. In addition, we know of 2 other of our patients in whom failures occurred, with subsequent pregnancy. The tubes, however, could not be secured for study. We have also seen functional failures in 2 patients in whom the lipiodol passed the site of crushing and ligation in one of the tubes but did not show any free spill in the peritoneal cavity in pictures made twenty-four hours later. Serial section studies of the removed segments, presented herewith, show the pathogenesis of some of the Madlener tubal sterilization failures. We have also studied the tube of one patient three days postoperative. We are submitting these findings in demonstrating how this method of tubal sterilization sometimes takes place, and for further testimony as to the uncertainty of this surgical procedure for obtaining tubal closure. No attempt was made to include a statistical study of the Madlener method of tubal closure.

CASE REPORTS

A. Histologic Study of Tubal Segments Where Pregnancy Followed the Sterilization.

CASE 1.—B. S., aged twenty-seven years, para ii, was sterilized by the Madlener method April 5, 1930, when a second low cervical cesarean operation was performed.

Her postoperative convalescence was normal, and the patient left the hospital in two weeks. Although the patient became pregnant again in the early part of 1931, she continued to menstruate up to June 18 of that year. A third elective cesarean section was performed on October 19, 1931, when a full-term baby was delivered. The fallopian tubes showed the following macroscopic changes (Fig. 1): both were markedly constricted at the site where they had been crushed and ligated, and there was a small, hard, semitransparent projection in the left tube where the remains of the silk suture, buried in the tissue, were visible. The suture remnant was likewise visible in the right tube where the constriction seemed complete; the left tube, however, appeared continuous and intact but curved slightly below the projected

Fig. 1.—Macroscopic appearance of tubal sterilization failure when segments were removed for serial section study as indicated by dotted lines. Left tube was patent and had reopened by a possible endosalpingiosis.

Fig. 2.—One end of segment showing the true endosalpinx above and the decidual-walled lumina below. (×24)

Fig. 3.—A larger magnification of decidual-walled lumina. The small lumen is lined by cuboidal cells and other lumina by flat epithelial cells. These hollow structures communicate with each other. (×100)

fibrotic portion toward the mesosalpinx. There was no gross evidence of fistulous openings in the tubes. The fimbriated ends were open. A segment of both tubes, each about one inch, at the site of the previously attempted sterilization, was removed and the cut ends were tied and inverted into the broad ligaments. The segments were studied by serial sections.

Histologic Examination.—Cross-sections at the ends of the left tubal segments (Fig. 2) reveal an opening containing the epithelial lining and folds characteristic of endosalpinx on the serosal aspect of the tube. Beneath this lumen, on the mesosalpinx aspect of the tube, there are two to four hollow structures lined by an

epithelium that is sometimes of flat cells and other times of cuboidal cells. Beneath the epithelium of these hollow structures are large cells resembling, if not identical with, decidual cells. These lumina vary in size and communicate with each other. Tracing these structures by serial sections it is seen that some end as diverticula, while others continue a parallel course, closely approximating the true endosalpinx lumen but no direct communication is noted. Serial tracings show the true endosalpinx becoming progressively smaller and eventually obliterated, whereas the hollow

Fig. 4.—Remnants of suture with giant cells and other evidences of foreign body reaction. (×420)

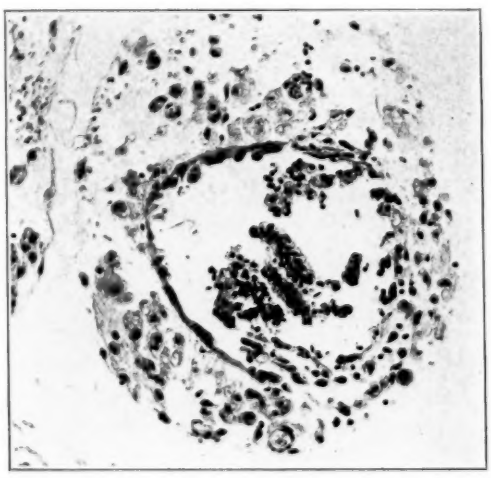


Fig. 5.—Remains of endosalpinx in the loop created by the Madlener operation. This lumen does not communicate with any of the others in the section. (×450)

structures with decidual-celled walls persist. Sections through the site of the projection in the midportion of the segment reveal that the endosalpinx has become completely interrupted, but the hollow structures, previously described, have reached their greatest size (Fig. 3). The projection itself shows remnants of the suture surrounded by much connective tissue, lymphocytes, endothelial cells, and many foreign body giant cells (Fig. 4). There are also numerous dilated capillaries and two thrombosed blood vessels. Just beneath this region, in an area of much

edema, is a small, tubular structure which is incompletely lined by cuboidal and columnar cells and surrounded by a basal membrane (Fig. 5). Even though it is devoid of a muscular coat, it can easily be interpreted as the remnant of the endosalpinx. It becomes progressively smaller and obliterated, but does not communicate with the decidual-like celled lumina which are seen in the same sections.

Although no communication between the decidual-walled openings and the true endosalpinx can be demonstrated, it seems reasonable for us to conclude that the former must have acted as oviducts and connected the tubal ends. Unfortunately, the segment removed for serial section was not large enough to demonstrate this (Fig. 6).

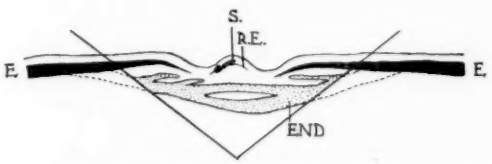


Fig. 6.—A diagrammatic sketch of the reopening of the tube by endosalpingiosis. *E*, endosalpinx; *End*, endosalpingiosis represented by hollow structures with decidual cell walls; *R.E.*, remnant of endosalpinx in loop created by the operation; *S*, remains of suture. Solid line shows segment of tube studied. The dotted line is the assumed communication of the decidual-walled lumina and the endosalpinx which was beyond the removed segment of the tube.

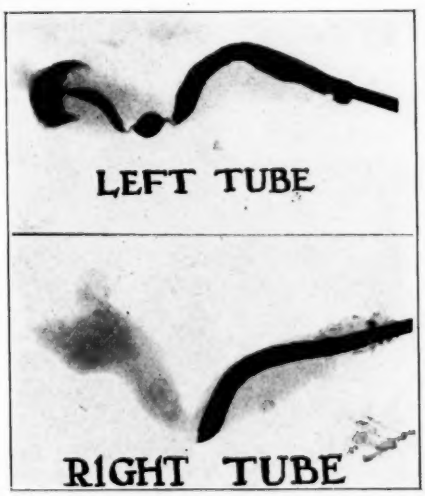


Fig. 7.—Lipiodol visualization of a segment of both tubes. The left was patent and the right was closed. (This picture was a useful guide in tracing the serial sections of the left tube.)

Sections of the right tube reveal that the lumen is completely occluded, with evidence of suture material surrounding it, in addition to foreign body giant cells and a chronic inflammatory reaction.

CASE 2.—E. F., aged thirty-one years, gravida iv, para ii, was sterilized on March 31, 1930, by the Madlener method when an extensive pelvic floor repair was made and an appendix was removed for subacute appendicitis. The patient left the hospital on the fifteenth day. There was a slight temperature elevation (98° to 100° F.) for the first three days, moderate abdominal distention for a short time, and some difficulty in voiding. Despite the sterilization the patient became pregnant again in about eighteen months and a cesarean section was performed because of

the previous extensive pelvic floor repair. Both tubes were excised in two-thirds of the length for study of failure of the tubes to remain closed. The removed segments of the tube were injected carefully with lipiodol through a blunt, soft needle point. The oil passed through the left tube readily but did not permeate the right tube. X-ray pictures of the patient's left tube show that it is made up of two main constrictions and a central dilatation (Fig. 7). Observing the tube from the uterine to the abdominal end one notes the tubal lumen narrowing to a

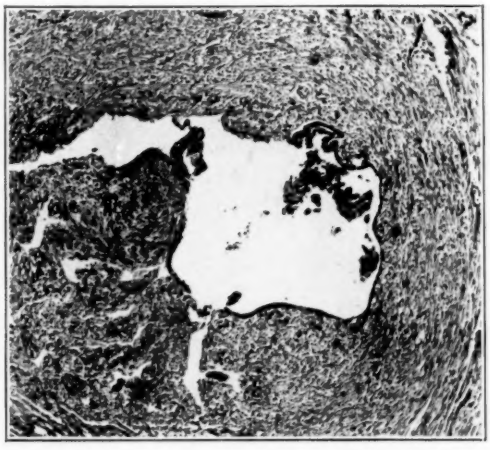


Fig. 8.—Granuloma projecting into the constriction of the tube nearest to the uterus. No foreign body was noted, but evidences of a chronic inflammatory reaction are seen. (×120)

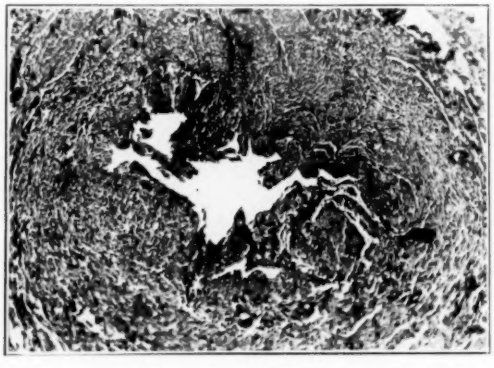


Fig. 9.—Another section through same constriction (Fig. 8). The lumen is lined with granulation tissue. (×120)

fine hair-line thickness followed by the dilatation, and then a second constriction which in itself contained a secondary narrowing.

Histologic Examination (left tube).—The lipiodol picture served as a useful guide for serial sections. Tracing the endosalpinx distally from the uterine end of the segment, the lumen, which is patent throughout its course, undergoes progressive constriction with gradual obliteration of the folds. As the lumen becomes constricted the lining epithelium is scanter and eventually is completely lost. In some sections a granuloma projects into the lumen of the tube (Fig. 8). It consists of a proliferation of endothelial cells, round cells, lymphocytes, and few multinuclear cells and plasma cells. Where constriction is most marked and the epithelium is

absent the lumen is lined by irregular granulation tissue (Fig. 9). The muscular wall is defective and the blood vessels are dilated. The lumen then undergoes progressive dilatation; small folds are again visible, lined by high columnar epithelial cells. The muscular coat is fibrotic and thicker on one side, so that the lumen has an eccentric position. In one portion there is a small decidual cell projection into the lumen. The lumen again becomes progressively smaller. The epithelium is more or less intact at the point of maximum constriction. The remains of the silk suture loosely encircling the lumen, are visible at this area (Fig. 10). The muscle wall is almost completely replaced by fibrous, connective tissue. In the vicinity of the suture remnants there is a marked foreign body reaction showing large giant cells, many fibroblasts and evidence of chronic inflammation. Where the lumen is extremely narrowed, the lining epithelium appears almost flat. Gradually the lumen once more dilates, the epithelium approaches the type normally seen in the tube, and the muscularis again becomes well formed.

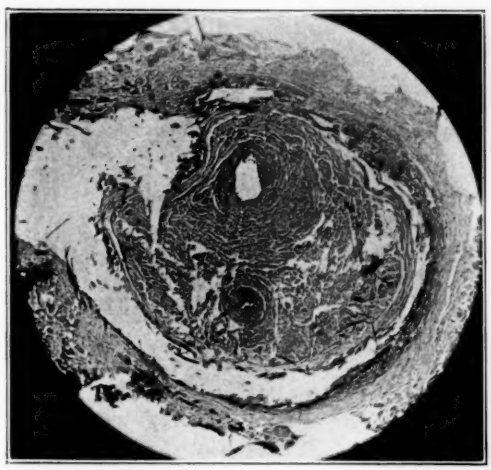


Fig. 10.—The suture surrounding the lumen in the constriction toward the fimbriated end of the tube. (×80)

B. Study of Madlener Sterilization Three Days Postoperative.

Through the courtesy of our pathologist, Dr. O. Saphir, we had the privilege of studying a Madlener tubal sterilization three days after the operation. The specimen was obtained at autopsy. One tube had been removed at the operation but the other had been crushed and ligated with silk. The segment showed a round projection above the ligature, which embraced two portions of the tube and a little of the mesosalpinx. The surface at the site of the operation was rough and opaque. The projection appeared hemorrhagic and bluish in color. Sections were taken through all portions of the tube. The tubes were cut in serial sections in the regions in which they were crushed and ligated. Distally and proximally to the crushing the sections show a marked passive hyperemia throughout. The mucosa is intact and bits of detached epithelium are seen within the lumen. The veins of the mesosalpinx are hyperemic and some contain recent thrombi. Sections through the areas of crushing stained poorly. *The folds of the lumen approximated one another but, nevertheless, it was nowhere completely obliterated.* The muscularis also stains poorly and reveals areas of hemorrhages. The portion of the tube which forms a loop between the sites of crushing showed partial necrosis and much hemorrhage.

C. Failures in Madlener Sterilization Visualized With Lipiodol.

CASE 1.—L. I., twenty-four years old, gravid. iii, para ii, was operated on October 22, 1929, when a right salpingo-oophorectomy, Baldy-Webster uterine suspension, and crushing and ligature of the left tube was done. The left ovary had multiple small cysts but was not removed. The patient had an uneventful post-

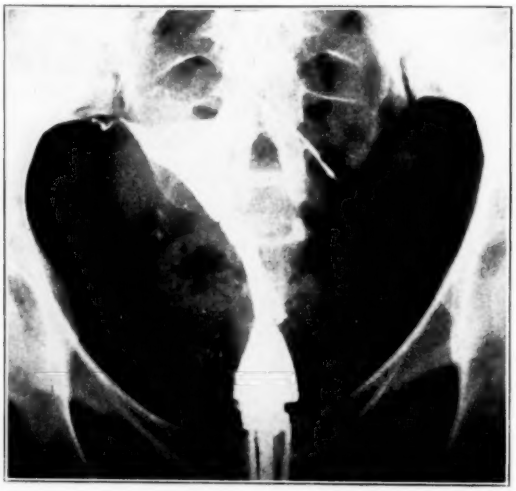


Fig. 11.—Roentgen lipiodol showing the oil passing the site of attempted closure (no free spill in picture made twenty-four hours later). Note a small portion of right tube visible beyond interstitial portion of tube. The tube had been removed up to the uterus. The angulated tract of oil is taken to be a sprouting of the tubal stump.

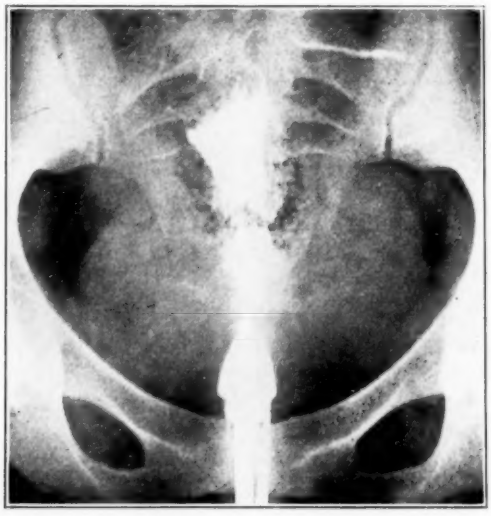


Fig. 12.—Roentgen lipiodol visualization of left tube up to fimbriated end. No free spill of lipiodol seen in picture made twenty-four hours later.

operative course and was discharged on the thirteenth day. She has not been pregnant again, up to the present date. A lipiodol injection performed on April 4, 1933, showed the interstitial portion of the right tube with a small sprout (endosalpingiosis?), and a left tube which is open up to the fimbriated end. There was no free spill of the lipiodol (Fig. 11).

CASE 2.—**E. Z., twenty-three years old, was sterilized by crushing and ligature of the fallopian tubes at the time of her third cesarean section on December 21, 1932. She has not become pregnant again, but a lipiodol injection on February 17, 1933, shows the left tube filled out to the fimbriated end without free spill into the abdominal cavity (Fig. 12).**

DISCUSSION

Although we have been able to study histologically only two instances of failures in the Madlener method of tubal closure, it is interesting that each case represented a different manner whereby the oviduct reconstructed itself. In the first case the tube was patent as the result of a "detour" around the original site of the operation. A sketch made at the time of the removal of the tube segments seems to illustrate this grossly. Remnants of the tube persisted in the loop created by the crushing and ligation, but nowhere was there communication with the newly formed oviduct. Portions of the original suture material with foreign body reaction were seen.

We believe that the approximation of the distal and proximal ends of the tubes was brought about by a union below the point of ligature and crushing. This probably occurred through the phenomenon of endosalpingiosis. Sprouts of tubal epithelium invaded the wall of each portion of the approximated tubes as a reaction to the operative trauma, and thus effected a union. Sampson stated that the misplaced tubal mucosa may assume the function of uterine mucosa. In the case studied this seemed very probable since the new lumina that were formed were surrounded by typical decidual cells, such as one would expect to occur in true endometrial tissue.

A study of the ends of the available segment shows a true tubal lumen with endosalpinx running parallel with the decidual walled lumina. Some of the latter ended blindly in the tube as diverticula, but those which persisted could not be seen communicating with the true tube in the segment that was removed. We feel that these large lumina with the decidual cells connected the tube proximal and distal to the site of crushing and ligation, and that the removal of a larger segment undoubtedly would have shown this. Certain it is, that a new oviduct had formed and that a fistulous connection with the peritoneum, which could have formed an avenue for the ovum, was absent. (Fig. 6.)

The histologic study of the next case is also interesting. A gross picture of the tubal channel was available through a lipiodol visualization of the segments. In the left tube which was patent, one sees that the distal and proximal ends of the tubes are connected through two areas of constricted and one dilated area. The constriction toward the uterine end of the tube represented a portion which was originally included in the crushing and ligation. Although the constriction was still present there was no evidence of the suture. The ligature apparently had cut through the tube gradually and the tubal wall had healed over in time

by granulation. A granuloma was still visible where this probably occurred. The dilatation at the center represented the loop that the Madlener operation created. The second constriction, particularly in its narrowest portion, was surrounded by the remains of the suture. This appeared to encircle the constricted lumen rather loosely. A foreign body reaction with giant cell formation was visible. No doubt the ligature which subsequently encircled only one portion of the fallopian tube, rather than two, was not sufficient to occlude completely the constricted tube. Muscle atrophy was definite at the site of crushing and ligation in both portions of the tube.

The two other cases, demonstrated by roentgen-lipiodol, illustrate the failures of the intended operation, although at present these tubes are closed at their fimbriated ends. These cases support the the findings of Fuchs and Lork, and Wolf. We are not certain why the fimbriated ends are closed, although Wolf contends that a progressive endosalpingitis closes the fimbria. It also is not certain whether or not these tubes will remain permanently closed at the fimbriated end. Perhaps this is just one step in the process of the reopening of the tubes.

In agreement with other observers we believe that the Madlener operation represents another attempted tubal sterilization procedure that fails. We would like to answer briefly the contentions of those who favor this operation, which in some respect holds for other methods of operative tubal sterility. These operations are most frequently attempted as a secondary procedure. The surgeon, therefore, is most often prompted to sterilize the patient when some other gynecologic operation is necessary. Such patients are likely to have reduced fertility. Likewise, sterilizations are usually performed after the patient has had a number of children, and has arrived at an age past her maximum fertility. Madlener reported in 1926 his operation on 119 patients, of whom 84, or slightly over 70 per cent, ranged from the ages of thirty-five to forty-eight. There is another factor that makes statistical surveys of any sterility operation difficult, namely, the loss of contact with the patients. Many patients who subsequently become pregnant were assured that this would not occur. They fail to report this . . . . to the surgeon who performed this operation, for more than one reason. If pregnancy does occasionally follow the bilateral salpingectomy with excision of the interstitial portion of the tube, and if none of the methods known have been proved by time to be free from subsequent failures, then tubal sterilization is always more or less insecure. For purposes of assurance, a lipiodol picture of the tubes should be taken after each operation for tubal sterilization. Only when the second picture, taken twenty-four hours later for determination of possible abdominal spill, is negative, should the operator feel that the patient is not likely to become pregnant. In cases in which the less absorbable suture material is used,

such as silk, another picture at a later date may be advisable. One can never be certain as to what changes the foreign body may ultimately bring about in the tube. Sampson regarded the behavior of the tubal epithelium in repair, to salpingectomy or tubal sterilization stumps as an exception to the rule governing the healing of operative wounds of hollow viscera. Bearing this in mind, and the clinical knowledge of how frequently the fallopian tubes undergo complete involution and resolution after inflammatory lesions, we have some basis for the understanding of tubal sterilization failures.

SUMMARY AND CONCLUSION

1. Two cases of failure of Madlener tubal sterilization with subsequent pregnancy were studied by serial sections. Each case represented a different manner whereby the oviduct function was restored. One tube appeared to have recovered its patency by a possible endosalpingiosis whereby an approximation of the tubes shunted the loop of crushing and ligation. The other tube recovered its function by the ligature cutting through one loop of the tube and encircled only the other portion of the tube, but with less constriction.

2. Two cases show by x-ray, lipiodol passing through the operated portion of the tubes on one side without a free spill into the abdominal cavity.

3. We believe that this operation is insecure in its original purpose and must be tested by lipiodol visualization at a later date. X-ray plays a useful rôle in checking up the results of the operation, and also in aiding the study of histologic segments of reopened tubes when they are removed.

REFERENCES

(1) *Pollak, John Osborn:* Practical Medicine Series, Gynecology Series 1930, p. 596, The Year Book Publishers, Chicago. (2) *Ries, E.:* Centralbl. f. Gynäk., 1897, p. 901. *Idem:* Am. J. Obst., January, 1898. (3) *Fraenkel, L.:* Arch. f. Gynäk. **58:** 374, 1899. (4) *Offergeld:* Ztschr. f. Geburtsh. u. Gynäk. **59:** 56, 1907. (5) *Leonard, V. N.:* Am. J. Obst. **67:** 443, 1913. (6) *Douglas, M.:* Surg. Gynec. Obst. **43:** 480, 1926. (7) *Polak, J. O.:* Am. J. Obst. **62:** 676, 1910. (8) *Zangemeister, W.:* Zentralbl. f. Gynäk. **52:** 411, 1928. *Idem:* Zentralbl. f. Gynäk. **54:** 718, 1930. (9) *Burckhard, G.:* Zentralbl. f. Gynäk. **52:** 1070, 1928. (10) *Lasch, C. H.:* München. med. Wchnschr. **71:** 552, 1924. (11) *Liepmann, W.:* Zentralbl. f. Gynäk. **51:** 2479, 1927. (12) *Kojima, G.:* Zentralbl. f. Gynäk. **52:** 1141, 1928. (13) *Köhler, M.:* Zentralbl. f. Gynäk. **52:** 1397, 1928. (14) *Nürnberg, L.:* Samml. klin. Vortr. Gynec., pp. 258-261, S. 33, 1917. (15) *Kalliwoda:* Arch. f. Gynäk. **113:** 565, 1920. (16) *Pokrowsky, W. A.:* La Gynec. **31:** 363, 1932. (17) *Madlener, M.:* Zentralbl. f. Gynäk. **43:** 380, 1919. (18) *Idem:* Zentralbl. f. Gynäk. **50:** 219, 1926. (19) *Wasser, B.:* Zentralbl. f. Gynäk. **49:** 2327, 1925. (20) *Bakscht, G.:* Monatschr. f. Gynäk. **83:** 71, 1929. (21) *Fuchs, H., and Lork, E. C.:* Monatschr. f. Gynäk. **88:** 199, 1931. (22) *Wolf, H.:* Zentralbl. f. Gynäk. **56:** 1383, 1932. (23) *Hadden, D.:* Am. J. Obst. **79:** 115, 1919. (24) *Rosenberger, C.:* Zentralbl. f. Gynäk. **52:** 1070, 1928. (25) *Sampson, J. A.:* Am. J. Obst. & Gynec. **20:** 443, 1930.

25 East Washington Street.
30 North Michigan Blvd.

DISCUSSION

DR. FRED A. ADAIR.—It would seem that this operation has been unsuccessful with a considerable number of persons because modifications of the original technic have been devised. The failures seem to have been due to regeneration of the tubal elements and to subsequent fistula formation. It seems that modifications in the technic also result unfavorably. If too much tissue is crushed, you may get a fistula formation; if not enough, you may get regeneration of the tubal elements. If tied too loosely, you may get a regeneration; if too tightly, you may get a necrosis with fistula formation.

I can report cases in which pregnancy subsequently occurred. These patients were not all operated upon by the same person, so that it is quite possible that the technic may have varied somewhat, but it shows that the failures are not due to individual technic at least. One patient because of a cardiac decompensation, had a hysterotomy at about the sixth week and both tubes were ligated. She made a good immediate recovery. She returned less than a year later again pregnant. A therapeutic abortion was performed by means of another hysterotomy. Both previous ligatures were in place and a fistula was present in the right tube. The tubes were resected and she has not been back since.

The other patient had a history of a tuberculous kidney which was removed. She also had tuberculous ulcerations of the bladder for several years. She was seen about four months prior to the date of delivery. She had a masculine pelvis. Cesarean section was performed and the tubes were ligated by means of the Madlener method. This operation was done in August, 1931. She returned to the hospital in 1932, pregnant again. This time, in order to avoid subsequent pregnancies, a hysterectomy was done. Both previous ligatures were seen. They were imbedded in the tubes and there was a fistula in one of the tubes.

It would seem from our results and from the failures of others in both this and other countries that there are too many possibilities of error in this operation to warrant its extensive use as a means of sterilization.

DR. EMIL RIES.—Evidently ligation, as in the Madlener operation, is not sufficient, no matter what material is used, whether absorbable or nonabsorbable, in the case of a small caliber muscular organ with epithelial lining, such as the tube. If the epithelium is crushed out completely, there is an approximation of the muscular coats. These do not heal together very well. That is the reason why even the apparently absolutely safe method of doing a wedge incision from the uterine horn on both sides with sutures is not absolutely satisfactory. The method we use now in the nonpregnant woman includes not only excision of a wedge of the uterine horn but also a covering of the suture line by the peritoneum of the bladder which we fold over and sew on the posterior surface of the body of the uterus, resulting in a peritoneal septum between the uterus and the peritoneal cavity. I have seen no pregnancies follow that method.

DR. C. E. GALLOWAY.—Silk holds the ends of the tubes in approximation, whereas No. 2 plain catgut will dissolve about the eighth day and the two ends of the tube will separate to a certain extent and peritonization will then take place over that raw surface.

This is a simple and time-saving method and should not be discarded, but, since these failures have occurred when silk was used, I would like to suggest substituting No. 2 plain catgut for the reasons mentioned above.

DR. FRED H. FALLS.—I ligate the tube about 2 cm. from the uterus, leaving the ends long. I then cut through the tube on the uterine side of the ligature and excise the proximal portion, going well into the horn of the uterus. I then take a

Barrett ligature carrier, pass it into the wound in the uterine cornu and bring it onto the surface of the uterus a short distance from the ligature on the tube. The ligature is then caught by the ligature carrier and the tied end of the tube is drawn into the uterine muscle and sewed in place. The wedge in the uterine cornu is then closed tightly. The other tube is treated likewise. There is no danger of hemorrhage from this operation.

FERTILITY IN THE MALE

II. Technic of the Spermatozoa Count

David L. Belding, M.D., Boston, Mass.

(From the Evans Memorial of the Massachusetts Memorial Hospitals)

IN THE study of fertility in the male various methods for determining the potency of the spermatozoa have been devised. Since no one test in itself is sufficient, it is obvious that an appraisal of fertility must be based on the combined results of several types of tests. Among these the spermatozoa count has been recommended by Macomber and Saunders[1] as one of the most reliable from the standpoint of ease of application and value in clinical interpretation. This paper deals chiefly with the technical requirements of this test.

TECHNICAL CONSIDERATIONS

The technic of Macomber and Saunders for recording the number of spermatozoa per cubic centimeter makes use of the white cell pipette, with a 1 to 20 dilution, and the ordinary blood counting chamber in the same manner as in making a blood count. Because variable results were obtained by this method in our hands a study of the various technical errors which affect the reliability of the spermatozoa count was undertaken. The errors due to sampling, dilution of the fluid, and technic of counting were determined by numerous counts on accurate dilutions of appreciable amounts of seminal fluid. As a result of these findings certain modifications in technic are suggested.

Seminal Fluid.—Spermatozoa are ejaculated in a vehicle consisting of a mixture of glandular secretions, largely prostatic and testicular. The proportion of these constituents varies in health and disease and according to the age, the individual, and the frequency of sexual intercourse. When first passed, the seminal fluid appears as a mixture of tenacious material and thin turbid fluid. On standing it loses this dual characteristic and becomes more homogeneous. The even distribution of spermatozoa depends upon the homogeneity of the mixture and upon its viscosity.

Diluting Fluid.—The bicarbonate-formalin solution used by Macomber and Saunders, consisting of 5 per cent sodium bicarbonate to which 1 per cent formalin had been added, proved entirely satisfactory as a diluting fluid. The bicarbonate by dissolving small amounts of mucus afforded an even distribution of spermatozoa. The formalin, by killing, rendered the spermatozoa immobile for counting and

acted as a preservative so that dilutions which were made from fresh semen could be counted at leisure without appreciable error.

Errors in Counting.—The variations in the spermatozoa count arising from the use of the counting chamber and the individual making the count were determined by a series of counts, using a standard dilution to avoid the error of sampling. Table I gives the results of 600 counts made upon 15 different specimens, an average of 40 per specimen. For comparative purposes these counts, which ranged from 51 to 200 million per cubic centimeter, have been reduced to a common average of 100 million. On this basis the standard deviation and the probable error of the mean for the counts on each specimen have been determined and the fluctuations in millions have been recorded.

TABLE I. VARIATIONS IN SPERMATOZOA COUNT DUE TO COUNTING TECHNIC

SPECIMEN	ACTUAL AVERAGE OF 40 COUNTS, NUMBER PER CUBIC CENTIMETER	STANDARD DEVIATION	PROBABLE DEVIATION	PROBABLE ERROR OF MEAN	PER CENT OF COUNTS SHOWING VARIATION FROM MEAN		EXTREME COUNTS (IN MILLIONS)	
					OVER 10 MILLION	OVER 20 MILLION	HIGH	LOW
1	99,185,000	15.52	±10.46	±1.66	45.0	15.0	130	48
2	72,055,000	10.77	± 7.26	±1.15	27.5	7.5	131	76
3	129,892,500	11.66	± 7.86	±1.24	42.5	12.5	122	73
4	109,262,500	11.45	± 7.72	±1.22	27.5	10.0	120	69
5	191,007,000	11.66	± 7.86	±1.24	42.5	10.0	127	64
6	76,815,000	15.07	±10.15	±1.61	50.0	27.5	134	67
7	180,470,000	8.47	± 5.70	±0.90	25.0	0.0	121	80
8	105,515,000	13.06	± 8.81	±1.39	37.5	15.0	133	72
9	51,862,500	9.73	± 6.55	±1.04	32.5	5.0	110	78
10	107,342,500	12.82	± 8.65	±1.37	45.0	5.0	128	67
11	200,560,000	7.23	± 4.87	±0.77	20.0	0.0	121	88
12	85,805,000	11.46	± 7.73	±1.22	47.5	5.0	120	74
13	92,587,000	8.53	± 5.75	±0.91	20.0	0.0	121	85
14	154,942,500	6.33	± 4.27	±0.68	12.5	0.0	130	79
15	136,337,500	10.68	± 7.20	±1.14	35.0	5.0	125	74

The great range between the extreme high count of 134 million and the extreme low count of 48 million shows that it is possible for a single count to be one-half of or one and one-third times the true count. Slightly over one-third of the counts fall outside a 10 per cent variation from the mean, and over one-ninth fall outside a 20 per cent variation. This means that one count in every three shows more than a 10 per cent error and one in every nine more than a 20 per cent error.

The wide range in the standard deviation indicates a marked difference between the 15 specimens in respect to the accuracy of the counts, even though a goodly number, 40, were made on each specimen. Inasmuch as the counts were made by the same technicians these results may be attributed either to daily variation in the mental attitude of the technicians or to differences in the seminal fluids.

The probable deviation indicates that in these 15 specimens one-half of the counts fall within a variation of ±4.27 per cent to ±10.46 per cent from the mean, averaging about ±7.6 per cent. In other words,

from the technic of counting an error of at least ±7.6 per cent is to be expected in half the counts. In order to have the probability that two counts come within this error, at least four counts should be made on each specimen.

Blood Counting Pipette vs. Bulk Dilution.—The method of counting the spermatozoa by the blood counting pipette method introduces the additional error of faulty sampling from the use of small quantities. Table II gives a comparison of the blood counting pipette and bulk dilution methods on nine specimens. The same dilution, 1:20, was used in both methods but larger quantities, 0.1 and 0.5 c.c. of seminal fluid, were employed for the bulk dilution method. The average number of spermatozoa and the standard deviation on the basis of an average count of 100 million are shown.

TABLE II. BLOOD COUNTING PIPETTE VS. BULK DILUTION METHOD

	BLOOD COUNTING PIPETTE	BULK DILUTION
Number of counts	85	91
Average number of spermatozoa per cubic centimeter	132,234,000	131,590,000
Standard deviation, on basis of an average 100 million count	11.22	9.21
Probable deviation	7.58	6.20
Per cent of counts showing variation		
over 10 million	34.1	20.9
over 20 million	10.6	4.4

The bulk dilution method gives more consistent results and consequently the count is more accurate than with the pipette method. The consistency of the seminal fluid apparently prevents the uniform distribution of the spermatozoa and renders sampling uneven because of the small amount taken in the blood counting pipette. About twice as many counts show variations of over 20 million with the blood counting pipette as with the bulk dilution method, and one and one-half times as many over 10 million.

The standard deviation is greater with the blood counting pipette, 11.22 vs. 9.21. The individual specimens with approximately 10 counts each show extremes of standard deviations ranging from 6.32 to 17.01 with the blood counting pipette and 4.24 to 13.53 with the bulk method of dilution, indicating differences in individual specimens. When spermatozoa are few both methods, particularly the pipette method, tend to give greater standard deviations; e.g., one specimen not included in this series, gave a standard deviation of 24.37 for nine counts with the blood counting pipette as compared with 12.55 for a similar number of counts with the bulk dilution method.

Small vs. Large Quantities for Dilution.—Dilutions of 1:20 which were made with 0.1 and 0.5 c.c. of seminal fluid are compared in Table III. There is little difference between the two quantities in the total count and standard deviation when accurate and well-sampled dilu-

tions are made. However, the use of the larger quantity, 0.5 c.c., is recommended, since for the ordinary laboratory it will give more reliable results.

TABLE III. QUANTITY OF SEMINAL FLUID DILUTED

	0.1 c.c.	0.5 c.c.
Number of counts	40	51
Total count	127,260,000	125,160,000
Standard deviation	9.40	9.09

Correct Dilution.—Since the bulk dilution method offers less opportunity for error than the blood counting pipette method, it is necessary to determine the dilution which will give accurate results. If the spermatozoa are too numerous in the counting chamber the count requires time and care and is usually too low. On the other hand, if the spermatozoa are too few the count will prove variable. A comparison of dilutions 1:20, 1:40, 1:80, and 1:100 is given in Table IV.

TABLE IV. DILUTION VOLUME

	DILUTION			
	1:20	1:40	1:80	1:100
Number of counts	149	150	150	149
Total actual count (per c.c.)	109,657,000	122,818,000	122,908,000	122,946,000
Standard deviation on basis of an average of 100 million	11.40	11.25	11.50	10.86
Extreme counts, in millions:				
High	115	117	111	114
Low	79	81	83	83
Per cent of counts showing deviation				
above 10 million	22.8	29.3	27.3	22.1
above 20 million	8.7	8.0	8.0	8.1

The standard deviation is practically the same for all four, and there is little difference between the variations above 20 million. When the spermatozoa average 123,000,000 per c.c. the dilution of 1:20 gives too low a count, but the other dilutions, 1:40, 1:80, and 1:100, give surprisingly comparable results. The count is most conveniently performed when about 256 spermatozoa are present over a square millimeter of the counting chamber. The optimum dilutions for counting are: 200 million – 1:80; 150 million – 1:60; 100 million – 1:40; 50 million – 1:20; 25 million – 1:10.

Probable error of the mean for the average dilution of 1:40 in terms of percentage of the total count is ±7.56 for one, ±3.78 for four, and ±2.52 for nine counts. Four counts are necessary to reduce the error substantially.

Proposed Technic for Counting.—As a result of this study the following technic is recommended:

1. The seminal fluid is thoroughly shaken to insure a homogeneous sample.

2. To 0.5 c.c. of the seminal fluid 9.5 c.c. of 5 per cent sodium bicarbonate containing 1 per cent of formalin is added.

3. A preliminary observation is made to determine the approximate number of spermatozoa.

4. The proper dilution is made from the original 1:10 so that about 16 spermatozoa are in each small square ($\frac{1}{16}$ square millimeter) of the blood counting chamber.

5. The average of four counts which approximately agree is taken.

GENERAL CONSIDERATIONS

Normal Count.—Macomber and Saunders found in 271 normal and abnormal individuals that the average number of spermatozoa per cubic centimeter was 100 million. Our average is slightly higher, 119 million for normal individuals and 70 million for sterile matings, but marked variations are encountered not only in different individuals but in the same individual at various times. A considerable range exists in so-called normal individuals; e.g., two men gave as the average of a series of counts 46 and 112 million per cubic centimeter.

The total number of spermatozoa in the emission is a more accurate method of expressing results than the number per cubic centimeter. The concentration of spermatozoa does not always indicate the total number of spermatozoa, which may be determined by multiplying the count by the volume of the seminal fluid. The proportion of prostatic fluid, testicular fluid, and spermatozoa varies at different times; e.g., Table VI shows that the same individual with a volume of 2.7 c.c. and a concentration of 177 million had almost as great a number of spermatozoa as with a volume of 5.5 c.c. and a concentration of 99 million. The total number of spermatozoa per emission averages between 400 and 600 million for healthy individuals.

Individual Variation.—Although an individual tends to maintain a fairly uniform level, if numerous counts are made over a period of several months a considerable range will be found. Extreme ranges of 33 to 258 million and 10 to 200 million have been encountered.

Table V shows the number of spermatozoa per cubic centimeter and the total number of spermatozoa per emission in a fertile individual over a period of five months. In this case the variation in spermatozoa is not associated with frequency of sexual intercourse. There is a faint suggestion of a seasonal fluctuation. The concentration and the total number of spermatozoa do not always agree, but they follow the same general trend. Among the varied and obscure causes which regulate the concentration and total number of spermatozoa are age, frequency of sexual intercourse, relative abundance of prostatic secretion, season, exercise, diet, mental strain, fatigue, activity of the endocrine glands, and various debilitating diseases.

Unfortunately it is impossible to determine from one or even two counts whether the number of spermatozoa represents the true level of the individual, a most important consideration for correct interpretation.

TABLE V. VARIATION IN NUMBER OF SPERMATOZOA IN ONE INDIVIDUAL

NUMBER	DATE	VOLUME OF SEMINAL FLUID IN C.C.	NUMBER OF SPERMATOZOA IN MILLIONS	
			PER C.C.	TOTAL
1	June 22	4.3	110.9	476.9
2	June 30	5.6	189.2	1059.5
3	July 6	7.0	90.2	631.5
4	July 8	3.0	98.8	296.5
5	July 25	2.2	75.0	165.0
6	July 28	4.6	54.1	248.9
7	August 2	4.2	51.4	215.9
8	August 5	4.0	118.6	474.3
9	August 10	3.6	133.9	482.0
10	August 17	4.0	64.1	256.5
11	August 22	3.9	112.9	440.3
12	August 26	4.3	139.9	601.6
13	September 1	5.2	258.0	1341.6
14	September 14	5.6	118.6	664.2
15	September 30	4.3	69.7	299.7
16	November 3	4.0	102.0	408.0

Frequency of Emissions.—The effect of frequency of sexual intercourse upon the number of spermatozoa is more pronounced in certain individuals. The spermatogenic capacity depends not only upon the individual himself but also upon age, food, habits of life, and physical condition. Certain individuals appear to have the power of sustained production, while others are quickly exhausted. Table VI shows the effect of a series of emissions at twelve-hour intervals on a man who had maintained an average well over 500 million per emission with intercourse at intervals of ten to fourteen days.

TABLE VI. THE EFFECT OF FREQUENT EMISSIONS UPON THE NUMBER OF SPERMATOZOA

NUMBER	HOURS	VOLUME OF SEMINAL FLUID IN C.C.	NUMBER OF SPERMATOZOA IN MILLIONS	
			PER C.C.	TOTAL
1	0	5.7	100.3	571.7
2	12	2.8	83.3	233.2
3	24	1.8	132.7	238.8
4	36	1.1	34.4	37.8
5	72	2.0	108.0	216.0
6	180	2.7	177.0	477.9
7	252	3.5	111.7	390.9
8	404	6.8	97.2	660.9
9	764	5.5	99.2	545.6

Recuperative processes compensated up to the third emission at twenty-four hours. The total spermatozoa then fell rapidly at thirty-six hours, and at forty-eight hours no emission was obtainable. The highest count per cubic centimeter was over five times that of the lowest. It will be noted that the concentration of the spermatozoa depends to some extent upon the volume of the discharge. In general the concentration trend follows that of the total number of spermatozoa.

Sexual Excitement.—The degree and duration of sexual excitement and the prolongation of the anticipatory period in the male have no apparent effect upon the total number of spermatozoa. A series of tests with and without prolonged sexual excitement gave practically the same volume of seminal fluid and the same number of spermatozoa. The end-result in both instances is merely the emptying of the seminal vesicles and the discharge of the accumulated secretions of the prostate and associated glands.

Value.—Macomber and Saunders consider that the spermatozoa count is a useful guide to fertility and that it is helpful in diagnosis, prognosis, and as a gauge of the efficiency of treatment. Our observations indicate that it is only an indirect indication of fertility. It is an index of the general spermatogenic activity of the testes, and as such is correlated with fertility so far as a good quantitative function is indicative of quality production. On the other hand, in many individuals the number of spermatozoa has no apparent relation to the abnormal morphology or to the vitality of the spermatozoa. Unless the number or the concentration is so materially lowered as to reduce mechanically the probability of insemination, the actual number of spermatozoa probably has little influence upon fertility. Owing to the variation in the number of spermatozoa from time to time in an individual, a single count may not give the true normal level.

SUMMARY

The technic of the spermatozoa count is discussed in regard to the errors involved in sampling, diluting, and counting. Because of faulty sampling, the bulk dilution method is superior to the blood counting pipette method. An improved technic for the spermatozoa count is presented.

The spermatozoa count is an index of spermatogenic activity and as such is correlated with fertility. A low count in itself does not necessarily indicate sterility or low fertility. Individual variation renders single counts of questionable value.

The writer wishes to acknowledge the technical assistance of Janet Ross and Minna Fogel.

REFERENCE

1. *Macomber, D., and Saunders, M. B.:* N. E. J. Med. 200: 981, 1929.

80 East Concord Street

THE SIGNIFICANCE OF MENSTRUAL DISTURBANCES IN PULMONARY TUBERCULOSIS*

Preliminary Report

H. Close Hesseltine, M.S., M.D., Chicago, Illinois
and
William M. Spear, M.D., C.M., Oakdale, Iowa

(From the Department of Obstetrics and Gynecology, State University of Iowa, and the Department of Obstetrics and Gynecology, The University of Chicago, and the Iowa State Sanatorium)

EVEN though some relationships and cross influences between pulmonary tuberculosis and menstruation have been reported by Alexander,[1] Beekmann,[2] Berki,[3] Caussimon,[4] Frank,[5] Jameson,[6] Kaufmann,[7] Macht,[8] Norris,[9] Novak,[10] and Rubin,[11] certain prognostic and therapeutic significances seem incomplete. Consequently, data were accumulated during the patient's stay at the State Sanatorium and later follow-up reports were instituted in order to learn more about these patients. The intention was, and is, to include all female patients from fourteen years (minimal age for admission) to the menopause, for a few years (averaging 100 or more annually), and then to follow them for several years. It is believed that this will allow not only better evaluations of various factors in prognosis, but also in treatment.

The patients in this series are citizens of Iowa and, excepting two colored persons, almost all are of western and northern European and British Isle stock. Fortunately, these patients tend to remain in their original communities, which permits a better follow-up by mail or by return trip to the institution.

In this present group of 148 patients with pulmonary tuberculosis, 18 have tuberculosis of other organs and 18 are in or through the menopause. Furthermore, those with altered menstruation are free from recognizable gynecologic or obstetric states, which might in any way be responsible for the symptoms. There is an estimated average latent period of six months from the onset of the first symptom until the patient is admitted to the sanatorium.

The following questions are typical of those which confront the phthisiologist, as well as the gynecologist. Does menstruation have an unfavorable influence upon the cause of the disease? What is the significance of amenorrhea and menorrhagia, and what are the indications for treatment in the latter? Is menstrual fever abnormal? Is its

*Read at a meeting of the Chicago Gynecological Society, June 16, 1933.

absence a good sign? Is there any prognostic difference between parous and nulliparous women? What prognostic or therapeutic guide can be obtained from menstrual alterations, types of menstrual fever, menstrual "color," and dysmenorrhea? Is irradiational or surgical therapy indicated to arrest menstruation in phthisical persons?

The degree of the chest lesion is expressed in terms used by the National Tuberculosis Association (minimal, moderately advanced, and far advanced). For prognosis the terms are: Favorable, guardedly favorable, and unfavorable, and these are followed as such unless death occurs. Even with a lapse of from two to five years for this study, no prognosis of cures is offered.

The menstrual behaviors are grouped into: (a) No change; (b) amenorrhea; (c) menorrhagia; (d) undetermined. (a) No change implies that no appreciable alteration has occurred. (b) Amenorrhea includes all those whose intermenstrual periods have become lengthened, or

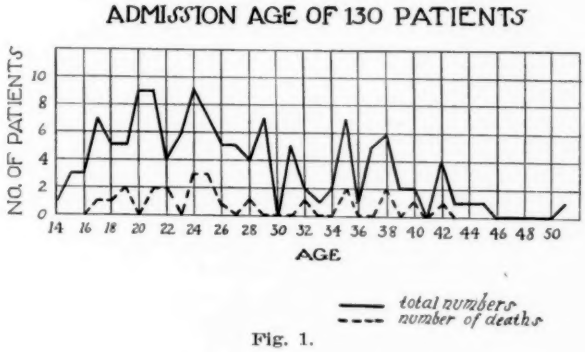


Fig. 1.

whose periods have become distinctly scant or ceased. (c) Menorrhagia represents those whose catamenia are distinctly more profuse, or have an appreciably shorter intermenstrual interval. (d) The undetermined group represents all those for which information is unsatisfactory, or who do not belong clearly to one of the other groups—perhaps most of them are normal. The menopause group includes all those in or past this period.

The graph of the total number of women having normal and altered menstruation is shown in Fig. 1. The age corresponds to that on admission. The dotted line is the mortality rate for the corresponding patients in actual numbers. The first peak, somewhat plateau in type, includes the teens and early twenties, while the other and sharper peak is restricted to the midthirties.

A special record card is used for abstracting data from the case record and the clinical course of the patient. The reverse side has space for follow-up notations. Some criticism may be offered against loose records, but these have facilitated the tabulations and studies.

The division of cases on the type of menstruation in patients free from organic pelvic disease shows no change in 45 (30.4 per cent), menorrhagia in 10 (6.7 per cent), amenorrhea in 63 (42.6 per cent), undetermined in 12 (8.1 per cent), and menopause in 18 (12.2 per cent) (Table I). Since we are not interested in the menopause group, the percentage for the unchanged, menorrhagia, amenorrhea, and undetermined groups are: 34.6, 7.7, 48.5, and 9.2, respectively, for the 130 women of menstruating age. The "no change" and the "amenorrhea" groups are classified further according to age, parity, and prognosis, while the other two divisions are too small to have any significance.

TABLE I. DIVISIONS FOR STUDY IN MENSTRUAL FLOW ALTERATIONS

MENSTRUAL FLOW	TOTAL GROUP		GROUPS STUDIED	
	NO.	PER CENT OF ENTIRE GROUP	NO.	PER CENT OF THOSE MENSTRUATING
Unchanged	45	30.4	45	34.6
Amount and/or frequency increased	10	6.7	10	7.7
Amount and/or frequency decreased	63	42.6	63	48.5
Character undetermined	12	8.1	12	9.2
Menopause—natural and artificial	18	12.2	—	—
Total	148		130	

TABLE II. CHEST LESION AND AGE OF ALL MENSTRUATING GROUPS

CHEST LESION	CONDITION	AGE DIVISIONS				TOTALS
		14-19	20-29	30-39	40-51	
Minimal	Favorable	3				7—No D*
	Guardedly favorable	2	1	1		
	Unfavorable					
	Dead					
Moderately advanced	Favorable		1	1		25—1D (4%)
	Guardedly favorable	1	7	6		
	Unfavorable	1	5	1	1	
	Dead		1			
Far advanced	Favorable					98—22D (22.4%)
	Guardedly favorable		2	1		
	Unfavorable	13	37	16	7	
	Dead	4	11	5	2	
Totals	Cases	24	65	31	10	130
	Mortality	16.6%	18.4%	16.1%	20%	—23D (17.7%)

*D = Dead.

In Table II the chest lesion and age divisions are listed. This reveals that for the minimal degree there are only 7 with no deaths. In the moderately advanced, 25 with one death, and 98 with 22 deaths in the far advanced division. In general, there is no particular difference between these degrees and the age incidence. Moreover, the total mortality incidence is almost parallel and varies less than 3 per cent

TABLE III. NO CHANGE IN MENSTRUATION

CHEST LESION	PARITY	AGE GROUP				TOTALS
		LESS THAN 20	20-29	30-39	40 AND OVER	
Minimal	Nulliparous	FF G				3
	Parous					
Moderately advanced	Nulliparous		GGG	GGG		6
	Parous		GG U			3
Far advanced	Nulliparous	UUUUUU DDD	G UUUUUUUUUU DD	UUU	U	26—5D
	Parous		U	UU D	UUU	7—1D
Total	Nulliparous					35—5D (14.28%)
	Parous					10—1D (10.0%)
						45—6D (13.3%)

F = Favorable; G = Guardedly favorable; U = Unfavorable; D = Dead.

TABLE IV. AMENORRHEA (HYPOMENORRHEA AND OLIGOMENORRHEA)—DEVELOPING

SYMPTOM APPEARANCE	CHEST LESION	PARITY	AGE GROUPS				TOTAL
			LESS THAN 20	20-29	30-39	40 AND OVER	
First	Minimal	Nulliparous	G				1
		Parous					
	Moderately advanced	Nulliparous					
		Parous					
	Far advanced	Nulliparous	UUU				3
		Parous		D			1—1D
Early to late	Minimal	Nulliparous	F				1
		Parous					
	Moderately advanced	Nulliparous	G	F U		U	4
		Parous			G		1
	Far advanced	Nulliparous	UUU	UUUUUUU D UUUU	U UUUUU		12—1D
		Parous		DD	D	D	13—4D
Late	Minimal	Nulliparous		G			1
		Parous					
	Moderately advanced	Nulliparous		G U D			3—1D
		Parous					
	Far advanced	Nulliparous	U	UUU DD UUUUUU	D UU	U	8—3D
		Parous	D	DDD	DD	D	15—7D
Total		Nulliparous					33— 7D (21.2%)
		Parous					30—10D (33.0%)
							63—17D (26.9%)

F = Favorable; G = Guardedly favorable; U = Unfavorable; D = Dead.

from the average mortality of 17.7 per cent. The highest incidence is in the age group of forty and over, with 20 per cent for 10 patients, which is too small a group to be important. It is interesting to note that 50 per cent (65 patients) of all menstrual groups are in the third decade, 18.1 per cent (24) in the second, and 23.8 per cent (31) in the fourth decade.

For no changes in menstruation, Table III records the groups in relation to age, parity, and degree of lesions, and according to prognosis. Nulliparous indicates that no pregnancies have occurred, while parous includes all women who have had gestations. There is no significant relationship of married and single women, but since questions relative to the seriousness of pregnancies predisposing to or aggravating the pulmonary lesions, other tables will be presented in a later communication. In general, the number is small, but perhaps trends may be noticed. At least five deaths in 35 nulliparous women means 14.28 per cent mortality, which is near the average. However, the total of all (45) present a mortality of 13.3 per cent.

In the "amenorrhea" group (Table IV), the mortality is double that of the "no change group," which represents 17 deaths in 63 patients (26.9

TABLE V. TEMPERATURE ALTERATIONS DURING MENSTRUATION

TEMPERATURE	CONDITION	MENSTRUAL CHANGE				TOTAL	
		NO CHANGE	AMENORRHEA	MENORRHAGIA	UNDETERMINED	CASES	MORTALITY
Increased 1° F. and over	Favorable						
	Guardedly favorable						
	Unfavorable		3*	2			
	Dead		2 (40%)			7	28.5%
Increased ¾° to 1° F.	Favorable						
	Guardedly favorable	2		1	3		
	Unfavorable	4	4	1	2		
	Dead	1 (14.3%)	1 (20%)			19	10.5%
Increased ⅕° to ½° F.	Favorable		1				
	Guardedly favorable	4	4				
	Unfavorable	15	15	4	5		
	Dead	1 (5%)	2 (9.1%)			51	5.8%
Not altered	Favorable	2	1		1		
	Guardedly favorable	5		1	1		
	Unfavorable	6*	16				
	Dead	4 (23.5%)	12 (41.4%)			49	32.6%
Lowered	Favorable						
	Guardedly favorable						
	Unfavorable	1	2	1			
	Dead					4	--
Totals	Cases	45	63	10	12	130	17.7%
	Mortality	13.3%	26.2%	--	--		

*One colored patient.

per cent), and in this group parous women (30) have 50 per cent more mortality (33 per cent) than the 33 nulliparous (21 per cent). Furthermore, the relationship of the onset of this symptom is interesting. When it was the first symptom, it occurred in 4 under twenty, and in 1 twenty-five-year-old patient, which is approximately 8 per cent. In 31 of the 63 patients, this was a moderately early sign, occurring after one or more other symptoms but before the diagnosis was established. The 27 remaining patients developed amenorrhea (usually scantier flow or cessation) only after the disease was well advanced. In some it might be looked upon as a terminal symptom. Because the menorrhagic and undetermined groups have only 10 and 12 patients, respectively, no table is presented.

Since the phthisiologist and the gynecologist may be concerned about menstrual fever, Table V is presented. Menstrual fever includes premenstrual (one to eight days) and/or menstrual interval. From this data, one might feel that either no temperature elevation, or a high fever, is an ill omen. The optimum seems to be $\frac{1}{5}°$ to $\frac{1}{2}°$ increase, either premenstrually or menstrually, while even an increase of $\frac{3}{5}°$ to 1° F. has only a 10.5 per cent mortality. Even though there may be evidence of advance of the pulmonary disease during the catamenia, control studies are indicated before it can be determined how serious a phenomenon menstruation may be. It is assumed, however, that it does not aid the patient. On the other hand, castration or subcastration therapy by roentgen ray, radium, or surgical intervention, may be even more serious.

TABLE VI. "COLOR" (HEMOPTYSIS, BLOOD-STREAKED SPUTUM, ETC.) DURING MENSTRUATION

	"COLOR"						
	DURING MENSES	NOT DURING MENSES	IRREGULAR	UNDETERMINED	TOTALS	NO "COLOR"	
No change in menses	G UUUU DD	G UUUU	U	--	13—2D (15.4%)	12.5% 4D—32	2F 8G 18U* 4D
Amenorrhea	F G UUUUU D	GG UUUU DDD	D	UU D	21—6D (28.5%)	26.2% 11D—42	1F 2G 28U* 11D
Menorrhagia	UUU	U	--	--	4—No D	No D—6	2G 4U
Undetermined	GG U	U	U	--	5—No D	No D—7	1F 2G 4U
Total cases	21	16	3	3	43	87	
Morbidity	14.2%	18.7%	33%	33%	18.5%	17.7%	

F = Favorable; G = Guardedly favorable; U = Unfavorable; D = Dead.
*One colored patient.

TABLE VII. DYSMENORRHEA WITH TYPE AND CHARACTER OF FLOW

AMOUNT OF FLOW	PARITY	MENSTRUAL CHANGE								TOTAL		
		NO CHANGE		AMENORRHEA		MENORRHAGIA		UNDETERMINED		DYSMENORRHEA		ALL CASES
		NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT OF TOTAL	
Moderate	Nulliparous	11 (3D)	36.6	12 (1D)	41.3	3	75.0	4	50.0	30 (4D)	42.2	71 (9D)
	Parous	5 (1D)	55.5	12 (3D)	46.1	3	60.0	2	66.6	22 (4D)	51.1	43 (12D)
		16 (4D)	41.0	24 (4D)	43.6	6	66.0	6	54.5	52 (8D)	45.6	114 (21D)
Scant	Nulliparous and parous	0		4		1		1		6	75.0	8
Profuse	Nulliparous and parous	2 (1D)		3 (1D)		0		0		5 (2D)	62.5	8 (2D)
Total	With dysmenorrhea	18 (5D)	40.0	31 (5D)	49.2	7	70.0	7	58.3	63	48.4	
										10D (15.8%)		
	Entire group	45		63		10		12				130
												23D (17.7%)

D = Dead.

TABLE VIII. DYSMENORRHEA—AGE AND DEGREE OF LESION

		LESS THAN 20		20-29		30-39		40-51				
Minimal	Dysmenorrhea	5	100.0%	0		1	100.0%	0		6		85.7%
	Total	5		1		1		0		7		
Moderately advanced	Dysmenorrhea	1	50.0%	10	71.4%	6	75.0%	1	100.0%	18		72.0%
	Total	2		14 (1D)		8		1		25 (1D)		
Far advanced	Dysmenorrhea	3 (1D)	18.7%	24 (4D)	47.0%	10 (3D)	45.5%	2 (1D)	22.2%	39 (9D)		39.7%
	Total	16 (4D)		51 (12D)		22 (4D)		9 (2D)		98 (22D)		
	Dysmenorrhea	9 (1D)	39.1%	34 (4D)	51.5%	17 (3D)	54.8%	3 (1D)	30.0%	63 (10D)	(15.8%)	(48.4%)
	All cases	23 (4D)		66 (13D)		31 (4D)		10 (2D)		130 (23D)	(17.7%)	

D = Dead.

Again, one may hear comments that "color" (blood-streaked sputum or hemoptysis) at the catamenia is an indication to arrest this periodic affair. In Table VI it may be noticed that the mortality rate is only 2 or 3 per cent among those having "color." The death rate is much greater in the "amenorrhea" than in the "no change menstruating" group. Such a minor difference as 2 or 3 per cent may be easily reversed with a large group. Moreover, the mortality is greater (4+ per cent) among those who had "color" only between menstruation, which observation will bear further study before much significance can be attributed to it.

An interpretation of painful periods and their association with pulmonary tuberculosis does not reveal much. In Tables VII and VIII, the painful periods increase with age up to the fifth decade. Dysmenorrhea is more common in parous women and also in scant and profuse flows than in the normal amounts. Although the numbers are small, there is a suggestion that the dysmenorrhea decreases as the degree of phthisis advances. There is no essential difference in the mortality rate among those with and those without dysmenorrhea. This series is yet too small to subdivide into premenstrual, menstrual, and postmenstrual symptoms in relationship to various factors.

SUMMARY AND CONCLUSIONS

This study was begun (1931) so that we might have better criteria for treatment of menstrual complications or menstrual alteration in pulmonary tuberculosis. The intention is to follow all patients in the childbearing period who enter the State Sanatorium at Oakdale over as many years as possible, evaluating from time to time prognostic signs and therapeutic procedures.

This small series permits no conclusions, but may indicate certain possible trends. It appears now that patients comparable to these are likely to have an increased mortality incidence if amenorrhea develops, especially late in the disease. An unexplained amenorrhea in young women may be the first symptom of phthisis. Menstrual temperature increase, not exceeding 1° F., appears to be a better prognostic sign than no thermal increase. Hemoptysis and blood-streaked sputum at menstruation are not associated here with a poorer prognosis than at other times. Dysmenorrhea appears more likely to occur in parous than in the nulliparous women, yet its incidence seems to decrease with the advance of the disease.

There has not been a sufficient number of patients observed (excluded from the above series), whose periods have been arrested by therapeutic means, to justify a report.

REFERENCES

(1) *Alexander, H.:* Schweiz. med. Wchnschr. **59**: 454, 1929. (2) *Beekmann, A.:* Ztschr. f. Tuberk. **52**: 273, 1928. (3) *Berki, B.:* Gyógyászat **70**: 894, 1930. (4) *Caussimon, J.:* Presse méd. **37**: 1561, 1929. (5) *Frank, R. T.:* Gynecological and

Obstetrical Monographs, Vol. XII, D. Appleton & Co., May, 1931, p. 88. (6) *Jameson, E. M.:* Am. J. Obst. & Gynec. 25: 22, 1933. (7) *Kaufmann, S.:* Ztschr. f. Tuberk. 53: 112, 1929. (8) *Macht, D. I.:* Am. J. M. Sc. 140: 835, 1910. (9) *Norris, C. C.:* Gynecological and Obstetrical Monographs, Vol. XI, D. Appleton & Co., New York, 1931, pp. 284, 288, 292. (10) *Novak, E.:* Gynecological and Obstetrical Monographs, Vol. II, D. Appleton & Co., New York, 1931, pp. 86, 87, 168, 169, 288, 289, 290, 292, 359. (11) *Rubin, I. C.:* Gynecological and Obstetrical Monographs, Vol. III, D. Appleton & Co., New York, 1931, p. 144.

5848 Drexel Avenue

THECA CELL TUMORS OF THE OVARY*

Perry J. Melnick, M.S., M.D., and Aaron E. Kanter, M.S., M.D., F.A.C.S., Chicago, Ill.

(From the Departments of Surgical Pathology and Gynecology, Cook County Hospital)

INTRODUCTION

In recent years Robert Meyer[1] has classified certain tumors of the ovary according to their clinical activity in altering the sexual characteristics of the afflicted person. In Meyer's classification we have two groups. The first consists of those tumors arising from the rete ovarii or medullary tubules (tubular adenoma; adenoma tubulare testiculare of Pick; arrhenoblastoma of Meyer) which masculinize the patients, causing excessive growth of hair on face, chest, and abdomen; deepening of the voice; masculinization of the facial expression; increase of the skeletal musculature; shrinkage of the breasts, etc.

The second group of tumors in Meyer's classification are those which arise from the granulosa cells of the follicle. These granulosa cell tumors in either their folliculoid or diffuse form usually have a feminizing action, producing glandular hyperplasia of the endometrium, more or less periodic bleeding from the uterus in postmenopausal women, and amenorrhea in younger women.

A third group of tumors, not described by Meyer, are those which arise from the cells of the theca interna. They were first reported in the literature in 1932 by Löffler and Priesel,[2] who named them fibroma thecocellulare xanthomatodes ovarii. The two cases here reported added to the six of Löffler and Priesel constitute the entire world literature on this type of tumor. These theca cell tumors are of the feminizing type, and like the granulosa cell tumors produce glandular hyperplasia of the endometrium, together with more or less periodic bleeding in postmenopausal women and amenorrhea in younger women.

The hormonal activity of these tumors makes them of special interest at the present time. The accurate methods of biologic assay of the female sex hormones developed in recent years by Stockard and

*Read at a meeting of the Chicago Gynecological Society, June 16, 1933.

Papanicolau,[3] Long and Evans,[4] and Allen and Doisy[5] have led to rapid strides in this field. Much work has been done and an extensive literature has appeared. Although many doubtful and controversial points have arisen, certain facts are fairly well established.

The best known hormone is the one produced by the ovary which has estrogenic properties, namely, it produces a characteristic hyperplasia of the genital tract in the experimental animal. It has been isolated in crystalline form (Doisy, Veler, and Thayer[6]). The names estrin, folliculin, theelin, and others have been proposed for this hormone; theelin has been accepted by the Council of Pharmacy and Chemistry of the American Medical Association.[7]

After theelin has produced a glandular hyperplasia of the endometrium, a second hormone produced by the corpus luteum, called progestin (Allen[8]), prepares the endometrium for the fertilized ovum. It produces the characteristic pregravid or premenstrual changes of the endometrium. Should fertilization fail to occur, the cycle starts again.

The periodic action of theelin and progestin is regulated by two hormones produced by the anterior lobe of the hypophysis. These anterior pituitary hormones are best known as Prolan A and Prolan B (Zondek and Aschheim[9]). Prolan A regulates the periodic discharge of theelin; Prolan B of progestin.

A great many properties of these hormones are as yet imperfectly understood. Their interrelationships, their many subsidiary actions, their occurrence in many different regions, and their site of origin are all questions in the process of being answered.

The site of origin of theelin has been one of the most discussed of these questions. The graafian follicle, particularly the granulosa cells (Allen, Doisy, and coworkers[5]) has been considered to produce the hormone. There is much evidence, however, that the cells of the theca interna play a rôle in its production. The rôle of the theca interna has always been something of a mystery. Its activity in the ripening follicle, in the young and degenerating corpus luteum, and in the atretic follicle, speaks eloquently for a possible function.

In the following report are described two cases of a newly recognized ovarian tumor which is derived from the theca interna cells. Since they exerted a distinct hormonal effect, it is believed that they strengthen the evidence that the theca cells take part in the production of theelin.

CASE REPORTS

CASE 1.—Mrs. A. D. was admitted to the gynecologic service of one of us (A. E. K.) on September 28, 1932. The Tumor Clinic diagnosis had been "suspect carcinoma of the cervix." Biopsy revealed no malignancy. The patient was a thin white female, seventy-two years of age, born in Denmark.

The chief complaint upon admission to the hospital was vaginal bleeding, which lasted three or four days. The patient described the bleeding as menstruation. This continued for one year, then stopped completely for about six months. On Sept. 23, 1932, she began to bleed again and continued to do so for three days. This was followed by some pain in the left side of the abdomen and both legs.

The past history was of no special significance. She had an operation on her right knee in 1897 with resulting ankylosis of the knee joint. She began to menstruate at the age of thirteen; the periods were regular every twenty-eight to thirty

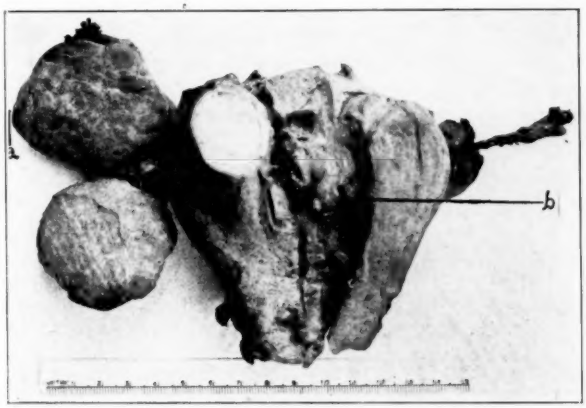


Fig. 1.—(Case 1.) *a*, Thecoma of ovary. b, Glandular hyperplasia of the endometrium with polyp formation.

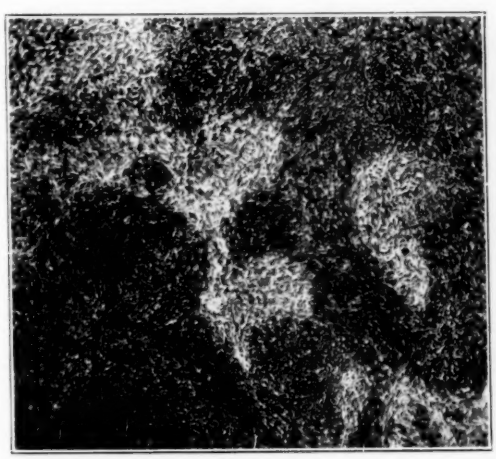


Fig. 2.—Thecoma of ovary (×150) stained with hematoxylin and eosin.

days, of four to five days' duration. She was married forty-five years ago and had been widowed twenty-five years. There were two normal full-term pregnancies with normal deliveries in 1891 and 1893. The onset of her menopause was in 1905. The family history was not known to the patient because she had been orphaned early in life.

The physical examination revealed a thin, aged, white female who did not appear acutely ill. Except for a patch of lupus vulgaris on the left cheek, and a hypertrophied and ankylosed right knee, there were no abnormalities found in the general examination. An internist called in consultation pronounced the heart and lungs

sound. The blood pressure was 140/80, the urine was negative for albumin and sugar, and the hemoglobin was 90 per cent. Vaginal examination revealed a narrowed menopausal vaginal canal with the cervix deep in the vault. The corpus uteri was irregularly enlarged and a tumor mass was felt on the left side which seemed to be a part of the uterus. The cervix, when visualized, showed a moderate erosion of the portio with endocervicitis. Because of the ankylosis of the right knee and the difficulties this might lead to in attempting to place the patient in the lithotomy position, vaginal hysterectomy was discarded in favor of total abdominal panhysterectomy. A preoperative diagnosis of fibromyomas of the uterus was made, with the possibility of carcinoma of the corpus to be considered.

On October 4, 1932, a total panhysterectomy was performed by the abdominal route under ether anesthesia. The operation was completed in thirty minutes and the patient left the operating room in good condition.

At operation it was found that there was a fibromyoma in the wall of the uterus. The left ovary, however, was of greater significance, being enlarged to the size of

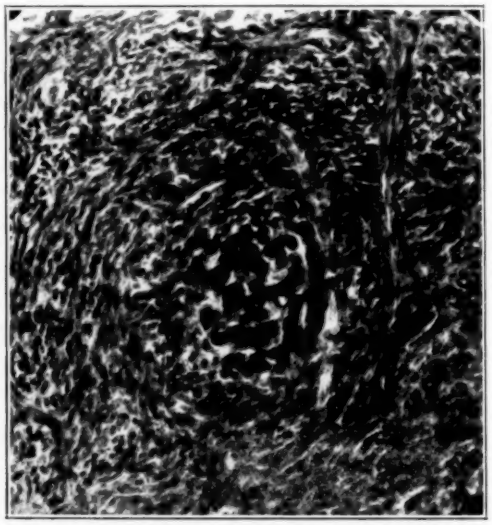


Fig. 3.—Thecoma of ovary (×600) stained with Sudan III and hematoxylin. A nest of epithelioid cells in the center. Lipoid droplets are abundant in all of the cells.

an orange, solid in consistency, and of a light yellow color. The right ovary was small and fibrotic. The uterus itself resembled that of a multiparous person, being much larger than one would expect to find in a woman who had been in the menopause for twenty-seven years.

The patient was apparently doing well on the evening of the day of the operation, but about midnight she went into collapse, turned cyanotic, had great respiratory difficulty, and the pulse became very weak. An attempt was made at venesection following a diagnosis of right heart failure, but the patient died before this could be accomplished. Permission for autopsy was not obtained.

Examination of Specimen (Fig. 1).—The uterus is enlarged, 12 by 8 by 6 cm., the wall 3 cm. thick, with a single intramural fibromyoma 2 cm. in diameter The endometrium is thickened, and in the fundus presents several soft polyps up to 2 cm. long. The cervix has bilateral scars. Both fallopian tubes are thin and patent. The right ovary is shrunken, wrinkled, and contains several hyalinized corpora albicantia. The left ovary is transformed into a solid firm tumor, 6 by 6 by 4 cm.

The surface is smooth and light yellow. The cut surface is striking. It is diffusely mottled with lobular bright yellow areas separated by thin septa of gray white connective tissue.

Histologic Examination.—The tumor of the ovary (Fig. 2) is composed of interweaving bundles of fusiform cells with delicate intercellular connective tissue fibrils, resembling a cellular fibroma. Septa of fibrous tissue traverse the tumor, giving it the lobulated appearance. The cells of the tumor have elongated nuclei which are regular; there are no mitotic figures. In places the cells change in character. They take on a distinct epithelioid appearance (Fig. 3). Even in these areas, however, there are still delicate intercellular collagen fibrils. Sections stained with Sudan III reveal the cytoplasm of both the fusiform and the epithelioid cells to contain an abundance of bright orange lipoid droplets which under the polariscope are doubly refractile, i.e., cholesterol and cholesterol esters. Microscopic examination of the endometrium (Fig. 4) reveals a marked glandular hyperplasia, with glandular polyp formation. The glands are tortuous, sometimes cystic, and are lined by an active high columnar epithelium. The stroma cells are swollen. The

Fig. 4.—(Case 1.) Glandular hyperplasia of the endometrium (×150) stained with hematoxylin and eosin.

hyperplasia is characteristic of the first half of the menstrual cycle, namely, that induced by the estrogenic hormone. The cervix showed a few areas of round-celled infiltration.

Diagnosis.—Theca cell tumor of the ovary. Glandular hyperplasia of the endometrium with glandular polyp formation. Intramural fibromyoma uteri. Chronic endocervicitis.

Case 2.—Mrs. M. S., a fifty-eight-year-old white woman, entered the Cook County Hospital on Dec. 11, 1932, with the complaint of uterine bleeding, of one year's duration. She had had regular and normal menstrual periods from the age of thirteen to her menopause which began ten years ago. She had four normal pregnancies with normal deliveries between thirty and twenty-four years ago. A year ago she began to have a bloody discharge. The bleeding was not profuse, and occurred at more or less irregular intervals. Two weeks before entrance she began to have a profuse hemorrhage which continued, and made her weak and dizzy. There was nothing else of significance in the past history.

Physical examination in general was negative, but on pelvic examination the uterus was thought to be large and nodular. The adnexa could not be made out.

A diagnosis of fibromyomas of the uterus was made; a possible carcinoma of the corpus was considered.

At operation one ovary was found to be converted into a solid light yellow tumor. A complete hysterectomy and bilateral salpingo-oophorectomy were performed. The patient made an uneventful recovery, and went home on the fourteenth postoperative day.

Pathologic Examination.—The specimen is a uterus with both fallopian tubes and ovaries. The uterus is enlarged, being 10 by 6 by 4 cm. in dimensions, and the wall 2 cm. thick. The endometrium is thickened, and in the fundus there are several soft polyps, measuring up to 2 cm. in diameter. The fallopian tubes showed no changes. One ovary is small and wrinkled; the other is transformed into a firm, solid tumor mass 6 by 4 by 4 cm. in dimensions. The surface is smooth and of a light yellow color. The cut surface is bright yellow and lobulated.

Microscopic examination of the tumor of the ovary (Fig. 5) reveals a structure almost identical with the first case. It is composed of the same type of fusiform cells, in many areas assuming an epithelioid appearance. Van Gieson stains here, too, reveal a delicate intercellular connective tissue, giving the a ppearance of a

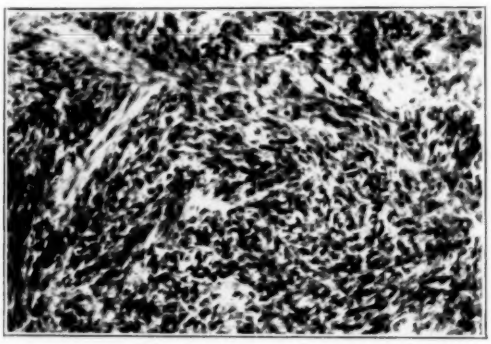


Fig. 5.—(Case 2.) Thecoma of ovary. The cells contain an abundance of lipoid droplets (×300) Sudan III and hematoxylin stain.

cellular fibroma. Sections stained with sudan III also reveal an abundance of lipoid droplets in the cytoplasm which are doubly refractile. The endometrium is also hyperplastic, with glandular polyp formation, of the same character as in the first case.

Diagnosis.—Theca cell tumor of the ovary. Glandular hyperplasia of the endometrium with glandular polyp formation.

DISCUSSION

These tumors occurred in women long past their menopause, who began to bleed again. In one case the bleeding was periodic and resembled the menstrual cycle. The uteri were not atrophic, as one expects at that age; and the endometrium in both cases was distinctly hyperplastic with glandular polyp formation. All these factors indicate a stimulating effect by an estrogenic hormone. The tumors undoubtedly secreted the estrogenic hormone which caused the bleeding and the hypertrophy of the uterus and the endometrium. The periodicity of the bleeding in the first case was probably not a true menstrual cycle because no corpus luteum was present, but it most likely

represents a reactivation of the anterior lobe of the pituitary by the secreted theelin, as Zondek[10] has demonstrated by injecting theelin in the senile mouse.

These tumors are composed of cells which have the histologic character of theca interna cells. Theca cell tumors have only recently been recognized. They have probably been heretofore confused with granulosa cell tumors which may produce a similar clinical picture. Wetterwald[11] in a discussion of postclimacteric bleeding due to ovarian tumors reported a granulosa cell tumor with doubly refractile lipoid droplets in the cytoplasm.

The theca cell tumors reported by Löffler and Priesel in 1932, consisted of a series of 6 cases collected over a period of eight years; 5 were benign and 1 was malignant. The gross appearance and microscopic structure of their tumors are very similar to the two cases reported here. Five of their 6 cases also occurred in women past the menopause, the ages being fifty-two, sixty-two, sixty-four, sixty-seven, and sixty-nine years. In only one of these was there uterine bleeding; but in 2 cases the tumors were incidental findings at autopsy and the gynecologic history may have been incomplete; in one case the uterus had been removed six years before the discovery of the tumor; and one was a malignant tumor. One patient was thirty-seven years of age and the tumor was discovered after nine months of amenorrhea. The cause of the amenorrhea in this case is of interest. It has been shown (Mazer and Goldstein[12]) that an excess production of the estrogenic hormone in a sexually normal woman will inhibit the progestin produced by the corpus luteum and prevent menstruation.

The lipoid content of the cells of these tumors might raise the question of a possible origin from the granulosa lutein cells. So-called "luteomas" supposedly derived from the granulosa lutein cells are rare. Sternberg[13] in Halban and Seitz's system of gynecology does not mention them. Kermauner[14] in Veit-Stoeckel's system reviews several cases. In general, these cases are associated with hirsutism and sexual precocity, and it is probable that they are really hypernephromas of the ovary (from misplaced adrenal rests or of teratoid origin) and are not derived from granulosa lutein cells. A recently reported case[15] also was associated with virilism, which disappeared after the tumor was removed.

The similarity of the hormonal effect of granulosa cell tumors and theca cell tumors suggests a possible relationship between these two types of cells. Such a relationship cannot be proved. Implanted granulosa cells do not induce estrus (Zondek and Aschheim[9]). The evidence to be produced here will show that the theca cells are probably concerned in the production of theelin. But it is possible that theca cells are formed under the influence of granulosa cells (Jaffe[16]). The granulosa cells of the developing follicle probably stimulate the immediately adjacent undifferentiated mesenchyma, and transform it into theca interna. If such is the case, the hormone in granulosa cell tumors is perhaps derived from the adjacent mesenchyma and not from the tumor cells themselves.

Löffler and Priesel concerned themselves mainly with the morphology of the theca cell tumors. The endocrinology of these tumors, however, is of great significance, and deserves careful analysis.

Two important questions must be answered. First, what characterizes the theca cells and theca cell tumors? Second, what function do the theca cells have?

The histology of the theca interna had for years been the subject of a lively controversy. At present, however, the consensus of opinion among histologists is as follows (Szymonowicz,[17] Corner,[18] Maximow and Bloom,[19] Schröder[20]): From the ovarian stroma around the developing follicle there differentiate two layers, the theca externa and the theca interna. The theca externa is not much different from the surrounding stroma. But the theca interna is different and more versatile. It becomes looser and very vascular. It is composed of fusiform cells with delicate intercellular collagen fibrils. Just before follicle maturation, however, these cells swell up and take on a distinct epithelioid appearance. After rupture of the follicle they enlarge still more, and their cytoplasm accumulates lipoid droplets. The granulosa cells now do the same thing, so that it is difficult by ordinary methods to distinguish between the two. But the granulosa cells soon enlarge to a greater extent and take on their characteristic lutein appearance. They are called granulosa lutein cells. The theca cells, now called theca lutein cells, remain somewhat smaller and more polyhedral, and are slightly separated from the granulosa lutein cells by a thin layer of connective tissue. They proliferate especially in the angles made by the folds of granulosa lutein cells, and send connective tissue and blood vessels into the center of the follicle to organize it. When the corpus luteum begins to degenerate, the theca lutein cells again proliferate, and finally complete its organization.

The theca cells are active during the process of follicle atresia also. Following degeneration of the ovum and of the granulosa cells the theca cells proliferate, enlarge, and accumulate lipoid, a pseudoluteinization. In the lower animals, where many follicles ripen at the same time followed by atresia, the theca cells blend extensively into the surrounding stroma. This has led to the term "interstitial tissue," used especially by Lipschütz.[21] The term is a poor one because it does not distinguish between other derivatives of the germinal epithelium, such as the medullary tissue. In human beings the theca cells are closely bound to the follicle.

Although both theca cells and granulosa cells are derivatives of the mesoderm, the granulosa cells have completely differentiated into an epithelial form. The theca cells, however, although able to assume an epithelioid appearance, retain their mesodermal properties. They are fusiform and have distinct connective tissue characteristics. Both theca lutein cells and granulosa lutein cells contain lipoid droplets. There is no agreement in regard to these lipoids, since they vary in different stages and in different animals. But in general, the character of the lipoid in each is different. Granulosa lutein cells contain mainly phospholipins; theca lutein cells contain cholesterol and cholesterol esters.

The tumors reported here are obviously composed of theca interna cells. They are characterized by a distinct connective tissue type of cell, which even in the areas where the cells take on an epithelioid appearance still have a delicate intercellular collagen reticulum; and by their content of cholesterol and cholesterol esters.

The next question to be answered is: What is the function of the theca cells? The evidence that the theca cells have a function, namely,

the production of theelin, has been accumulated during the process of studying the anterior pituitary hormones. But because of the great significance of these latter hormones in the control of the ovarian cycle, the theca cells have remained in the background. The very interesting logical steps which led to the discovery of the anterior pituitary hormones are worth reviewing, because they also demonstrate the part which the theca cells play.

The fact that the estrus cycle coincides with the periodic ripening of the follicles led to the very natural assumption that the follicle produced theelin. Allen and Doisy and their coworkers[5] and others maintain that the granulosa cells produce the hormone. Trendelenburg[22] states that it can no longer be doubted that the estrus-producing hormone arises primarily from the follicle. Evidence gradually accumulated, however, that the maturing graafian follicle is not the cause of estrus, but that the estrus-producing stimulus causes follicle maturation as well as the other phenomena of estrus.

First, it is known that if bilateral oophorectomy is performed in a rodent two days before estrus begins, histologic examination of the ovaries shows no ripening follicles; yet the succeeding estrus cycle will still occur. This appears to indicate that the estrus-producing stimulus begins at least two days before the actual occurrence of the cycle, and that it has no relation to ripe follicles (Parkes[23]).

The next step would be to eliminate the graafian follicles and observe the effect on the estrus cycle. This has been done by various procedures:

a. In 1920, Blair Bell[24] grafted into castrated animals parts of ovaries from which the cortex with the follicles had been removed, leaving only stroma and interstitial tissue, that is, theca cells. The normal estrus cycle was established.

b. Whole ovaries, or parts of ovaries including graafian follicles, when grafted into castrated animals, result in establishing the normal estrus cycle. When such grafts are removed and studied histologically, they are seen to have undergone a profound change. Practically all workers, from Ribbert[25] to the present time (Marshall,[26] Steinach,[27] Athias,[28] and others) are agreed that such grafts undergo extensive follicular atresia. The follicles are replaced by masses of theca cells.

c. However, the really conclusive experiments consisted of eliminating the follicles by means of x-ray. This was done by Steinach and Holzknecht,[29] Lipschütz,[21] Bouin, Ancel and Villemin,[30] and Hüssy and Wallart,[31] who found, in general, that the proper dosage resulted in follicular degeneration and atresia, with marked proliferation of the theca cells. The ovaries are converted into masses of theca cell derivatives, and yet had definite hormonal activity. Parkes and coworkers[23] and later Zondek[10] found in addition the remarkable result that although there was a complete elimination of all the cyclic changes in the ovary, the estrus cycle was in no way interfered with.

Zondek[10] performed an ingenious converse experiment. By feeding thallium to mice, the estrus cycle was completely eliminated. Yet the ovarian cycle remained intact, follicles ripened, and corpora lutea formed in the normal manner.

The final link in the chain of evidence is furnished by Foa's[32] work. He had found that an ovary from an immature animal grafted into a mature one matured

very rapidly and began to ripen follicles; vice versa, an ovary from a mature animal grafted into an immature one became quiescent.

Apparently the age of the ovary is governed by the age of the body. Some somatic influence outside the ovary controls its periodicity. Theelin is probably secreted by the ovary at a more or less constant rate, but its periodic discharge is governed by some external factor. This external factor was discovered to be the anterior pituitary hormones. The classical experiments by Zondek and Aschheim[9] and by Smith and Engle[33] in 1927 are well known.

The prominence of the theca cells in these experiments cannot be disregarded. Steinach[27] and Lipschütz[21] had early emphasized their importance. Lipschütz even considers them to be the main endocrine tissue of the ovary. Zondek and Aschheim[34] became interested in this concept, and in an elaborate series of experiments proved that the theca cells secrete theelin. By implanting various structures composed of these cells into castrated animals they established the normal estrus cycle. By careful dissection they isolated the theca cell layers from the follicles of human ovaries and implanted them, with the expected result. They also dissected out the wall of a theca lutein cyst from a human ovary, with the same result on implantation. During the latter part of pregnancy there is extensive follicular atresia and therefore theca cell proliferation. Implanted ovarian cortex of ovaries removed during pregnancy also established the normal estrus cycle. Implanted granulosa cells do not induce estrus.

There is more evidence of a miscellaneous nature which indicates that the theca cells are concerned in the production of theelin. (a) During pregnancy there is a large amount of theelin in the blood and urine. The young corpus luteum has an active complement of theca cells which may be a factor. Zondek[10] has shown that the young corpus luteum contains large amounts of theelin, but none when it degenerates. During the latter part of pregnancy when the corpus luteum degenerates, extensive follicular atresia sets in, which again furnishes theca cells (Fellner[35]). (b) In the newborn infant the mammary glands often secrete, there are follicles in the ovary, and the uterus is well developed. These activities soon subside, and the uterus shrinks in weight (Trendelenburg[22]). This cannot be due to a maternal hormone, since Parkes[23] has shown that the placenta is an effective barrier. But during late fetal life and early postnatal life there is extensive follicular atresia which may furnish theca cells to produce the phenomenon. (c) Collip[36] found in the immature hypophysectomized rat injected with his anterior pituitary-like hormone from the placenta, that the normal estrus cycle was established. Examination of the ovaries revealed them to be composed of masses of theca cells, no ripe follicles being formed.

Enough examples have been given to illustrate the activity of the theca cells. The hormonal activity of the theca cell tumors reported here furnishes additional evidence that these cells produce the estrogenic hormone.

SUMMARY

Certain ovarian tumors exert hormonal effects, and of the feminizing type there are two, the granulosa cell tumors and the theca cell tumors. Theca cell tumors have only recently been recognized. Two such cases are reported. They produced hyperplasia of the myometrium and endometrium, and postclimacteric bleeding. In one case the bleeding was periodic, resembling the normal menstrual cycle. The tumors are composed of cells which have the histologic character-

istics of theca interna cells. Apparently these tumors secreted theelin. This conclusion is supported by much experimental and deductive evidence from the literature that the theca cells secrete the estrogenic hormone.

Unfortunately, the tumors were formalin fixed before implantation experiments could be made, and no blood or urine tests for hormone were made, but perhaps future investigators may be able to do this, for diagnosis as well as for investigation. In this connection we reiterate an admonition made in a previous communication,[37] namely, if in a woman past the menopause who is bleeding, nothing of an etiologic nature is found in the systemic or local examination, and curettage proves barren, one should perform a colpotomy and visualize the ovaries, in order that guilty ovarian tumors be not overlooked.

310 South Michigan Avenue

REFERENCES

(1) *Meyer, R.:* Am. J. Obst. & Gynec. **22:** 697, 1931. (2) *Löffler, E., and Priesel, A.:* Beitr. z. path. Anat. u. z. allg. Path. **90:** 199, 1932. (3) *Stockard, C. R., and Papanicolau, G. N.:* Am. J. Anat. **22:** 225, 1917. (4) *Long, J. A., and Evans, H. M.:* Mem. Univ. Calif. **6:** 1, 1932. (5) *Allen, E., Doisy, E. A., and coworkers:* Am. J. Anat. **34:** 133, 1924. (6) *Doisy, E. A., Veler, C. D., and Thayer, S. J.:* J. Biol. Chem. **88:** 499, 1930. (7) Report of Council of Pharmacy and Chemistry, American Medical Association, J. A. M. A. **100:** 1331, 1933. (8) *Allen, W. M.:* Am. J. Physiol. **92:** 174, 1930. (9) *Zondek, B., and Aschheim, S.:* Arch. f. Gynäk. **130:** 1, 1927. (10) *Zondek, B.:* Die Hormone des Ovariums und des Hypophysen-Vorderlappens, Berlin, 1931, Julius Springer. (11) *Wetterwald, M.:* Schweiz. med. Wchnschr. **58:** 39 and 298, 1928. (12) *Mazer, C., and Goldstein, L.:* Clinical Endocrinology of the Female, Philadelphia, 1932, W. B. Saunders Co. (13) *Sternberg, C.:* Geschwülste des Eierstockes, Biologie und Pathologie des Weibes, Halban und Seitz, Berlin, 1926, Urban u. Schwarzenberg, Vol. 5, part 2, p. 675. (14) *Kermauner, F.:* Die Erkrankungen des Eierstockes, Handbuch der Gynäkologie, Veit-Stoeckel, Munich, 1932, J. F. Bergmann, ed. 3, Vol. 7, p. 1. (15) *Casacesco, A., Draganesco, St., Georgesco, M., and Dinischiotu, G. T.:* Presse méd. **39:** 1264, 1931. (16) *Jaffe, R. H.:* Personal communication. (17) *Szymonowicz, L.:* Lehrbuch der Histologie, Leipzig, 1924, Curt Kabitzsch, p. 307. (18) *Corner, G. W.:* Cytology of the Ovum, Special Cytology (Cowdry), New York, 1932, Paul B. Hoeber, Vol. 3, p. 1567. (19) *Maximow, A. A., and Bloom, W.:* Text-Book of Histology, Philadelphia, 1930, W. B. Saunders Co., p. 635. (20) *Schröder, R.:* Weibliche Genitalorgane, Handbuch der mikroskopischen Anatomie des Menschen, V. Möllendorf, Berlin, 1930, Julius Springer, Vol. 7, Part I, p. 329. (21) *Lipschütz, A.:* The Internal Secretions of the Sex Glands, Baltimore, 1924, Williams and Wilkins. (22) *Trendelenburg, P.:* Die Hormone; Ihre Physiologie und Pharmakologie, Berlin, 1929, Julius Springer. (23) *Parkes, A. S.:* The Internal Secretions of the Ovary, London, 1929, Longmans, Green and Co. (24) *Bell, Blair:* The Sex-Complex, New York, 1920, William Wood & Co. (25) *Ribbert, H.:* Arch. f. Entwcklngsmechn. d. Organ. **7:** 688, 1898. (26) *Marshall, F. H. A.:* The Physiology of Reproduction, ed. 2, London, 1922, Longmans, Green and Co. (27) *Steinach, E.:* Arch. f. Entwcklngsmechn. d. Organ. **42:** 307, 1916. (28) *Athias, M.:* Compt. rend. Soc. de biol. **88:** 1315, 1923. (29) *Steinach, E., and Holzknecht, G.:* Arch. f. Entwcklngsmechn. d. Organ. **42:** 490, 1916. (30) *Bouin, P. J., Ancel, P., and Villemin, F.:* Compt. rend. Soc. de biol. **61:** 417, 1906. (31) *Hüssy, P., and Wallart, J.:* Ztschr. f. Geburtsh. u. Gynäk. **77:** 177, 1915. (32) *Foa* (quoted by Parkes[23]). (33) *Smith, R. E., and Engle, E. T.:* Am. J. Anat. **40:** 159, 1927. (34) *Zondek, B., and Aschheim, S.:* Arch. f. Gynäk. **127:** 250, 1926. (35) *Fellner, O. O.:* Monatschr. f. Geburtsh. u. Gynäk. **54:** 88, 1921. (36) *Collip, J. B., Selye, H., Thomson, D. L.:* Proc. Soc. Exper. Biol. & Med. **30:** 647, 780, 1933. (37) *Kanter, A. E., and Klawans, A. H.:* Postmenopausal Bleeding, Am. J. Obst. & Gynec. **24:** 192, 1932.

CONTRACEPTION—A NEGLECTED FIELD FOR PREVENTIVE MEDICINE*

OWEN JONES TOLAND, M.D., PHILADELPHIA, PA.

IN THE last few years "birth control" has ceased to be a controversial topic among the majority of medical practitioners of this country. The New York Academy of Medicine has gone on record as expressing its approval, and a recent canvass of the entire membership of the Pennsylvania State Medical Society has revealed that 90 per cent of those who replied are in favor of modifying our existing state laws on this subject to the extent of permitting contraceptive advice to married women for "health preservation" reasons.

The advent of the vaginal diaphragm and jelly method has inaugurated a new epoch in this branch of medicine. It has been proved conclusively from several large and well-studied series of cases that no maternal damage can result from the employment of this particular method, and that, furthermore, even its prolonged use does not tend to cause sterility. With these two major objections, which applied to many of the older contraceptive methods (particularly the use of the intracervical pessaries) swept aside, the large majority of the medical profession of this country has come more and more to regard contraceptive practice in its true light; that is, not as a moral issue, but rather as a branch of preventive medicine, for the following excellent reasons:

It is an established fact that pregnancy is a serious, often fatal complication of many organic diseases, notably valvular heart disease, tuberculosis, diabetes, chronic cardiorenal disease, and others. A married woman suffering from such organic disease should be entitled to medical advice which will protect her from pregnancy just as much as citizens should be told how to protect themselves from smallpox, diphtheria, or typhoid fever. The same line of reasoning applies to women who have just completed a pregnancy complicated by eclampsia, severe hemorrhage, puerperal sepsis, etc. This group should certainly, from a purely medical point of view, be protected from pregnancy until such time as they are judged physically fit to bear another child.

Further, it is common observation that pregnancies, repeated at frequent intervals, have a most deleterious effect upon mothers as a whole. Of course the occasional woman is strong enough to stand the strain of eight to twelve pregnancies occurring one after the other without apparent damage to health, but she is an exception. The picture of the

*Read at stated meeting of the Obstetrical Society of Philadelphia, May 4, 1933.

thoroughly depleted woman in her late twenties, or early thirties, who has had five, six, or seven pregnancies in rapid succession is unfortunately a much more familiar and distressing one. Such a woman is usually worn out both mentally and physically, and looks as if she were in her late forties.

In order to determine just what percentage of women are being discharged from our city maternities, who might be considered as fit candidates for this particular form of medical advice, I made a study of one thousand case records taken at random from the files of the Philadelphia Lying-In Hospital. This institution is quite representative of the average big city maternity hospital.

These thousand cases are all of patients discharged from the maternity wards after a full-term delivery. All private case histories are excluded, because effective contraceptive practice is already widespread among this group. All gynecologic records are excluded because, in the first place, many of these patients were unmarried, and many others were past the childbearing age.

The patients seemingly entitled to receive contraceptive advice as a routine part of their puerperal care—as a matter of fact no such advice is given in this hospital—fall easily into three main groups. The first group consists of women discharged suffering from serious organic disease, who should permanently, in all probability, not be subjected to another pregnancy. The second consists of women who have had the last pregnancy or delivery complicated by some serious and debilitating condition, and who should not be subjected to another pregnancy until adjudged fit by medical examination. The third group, and by far the largest, comes under the head of what might be termed a "child spacing" indication. It is obviously difficult to draw up a rigid set of indications that will fit the needs of all patients in this respect, but those enumerated later represent a consensus of opinion of most of the staff of the hospital, as being reasonable and what they would recommend to their own private patients; and it must be remembered that the underlying idea is the prevention of serious depletion rather than the relief of an already seriously depleted person.

There were only sixteen patients out of the thousand who fell into the first group. Seven had quite severe valvular heart disease of rheumatic origin; eight had proved active pulmonary tuberculosis, and one was a diabetic requiring insulin. Thus we see while the individual members of this group are in urgent need of care, the group itself is small.

There were only twelve in the second group. Four of these had eclampsia; one had very severe toxemia of late gestation requiring induction of labor at the seventh month, but who did not have convulsions; one, with pernicious vomiting, had to have pregnancy terminated at the fifth month; two patients had second cesarean section performed,

both sections being only two years apart; two patients had ruptured ectopic gestations; one had severe pleurisy with effusion requiring several tappings during the later months of pregnancy; one patient was operated upon for an ovarian cyst during the fourth month, and miscarried a few days after the operation and was very ill. The same general remarks may be made of the group.

The last group, whose indication was child spacing, was large—369 in all. It should be said before going into the subsections of this group that miscarriages occurring therein were not counted, mainly because I felt that the histories, taken as they are in the hurried crowded prenatal clinic, are too inaccurate in this respect. Women frequently forget early miscarriages and are reluctant about induced abortions, and many patients do not speak English well enough to give an accurate account. It seemed to give a truer picture to rule miscarriages out altogether, though unquestionably this tends to make our figures err on the conservative side.

Another factor that makes this study understate, rather than overstate, the actual need for this type of care is the fact that rapidly repeated pregnancies have the most depleting effect on the mother, and there is no way of always telling this on our records. On our charts at the Lying-In Hospital the number of years married and the ages of previous children are not stated—a serious omission. Thus, assuming that a woman was married at twenty-six and had four pregnancies by the time she was thirty-two, she would obviously be in need of contraceptive advice, but would not be entitled to it under the indications to be given shortly. These indications are based on the supposition that our ward patients are married in their late teens or early twenties, which, as a matter of fact, most of them are.

The first subsection consists of women twenty years old, or younger, who had two full-term pregnancies or over. There were 105 cases. The next subsection is made up of women twenty-five or under, who had three full-term pregnancies or over. There were 86 such cases. The next subsection is of women thirty or under, who had four full-term pregnancies or over. There were 50 such cases. The last subsection is made up of women who had had five full-term pregnancies, regardless of their age, which accounts largely for the smallness of the third and fourth groups. There were 128 such cases. The total for the entire group is 369 cases, or 36.9 per cent of the total who needed contraceptive advice for child spacing. In this study all sorts of reproductive absurdities were uncovered, such as one record of a nineteen-year-old girl with five living children, and one twenty-eight-year-old woman who had already had nine full-term pregnancies.

It is true that up to date our hospitals have not availed themselves of the opportunity to give this type of advice to their patients, but

things move slowly, and perhaps the day is not so far distant when the needs of parturient women in this particular respect will receive attention as a matter of routine in our postnatal clinics just as their prenatal complications do today.

SUMMARY

One thousand records of patients discharged from the maternity wards of the Philadelphia Lying-In Hospital were studied to see in what proportion of cases contraceptive advice might be necessary as a part of postpartum care.

From this study it is apparent that such advice could have been given, at a conservative estimate, to 397 women out of one thousand, approximately 40 per cent.

By far the most usual indication is for child spacing, and not for organic disease or acute complications of the last pregnancy, which groups are only 1.6 and 1.2 per cent, respectively.

The figures, particularly on child spacing, are a most conservative estimate, inasmuch as miscarriages are not counted.

CONCLUSION

Maternity hospitals, in failing to give contraceptive information to patients needing such advice, are neglecting a branch of preventive medicine whose need is urgent and that has a wide field for usefulness.

The author is indebted to Dr. Edmund B. Piper and Dr. Norris W. Vaux for the privilege of using their ward histories in making this study.

323 South Twentieth Street.

DISCUSSION

DR. JOHN A. McGLINN.—When it seems probable that the health or the life of a woman is threatened by the advent of pregnancy, it is not only the right but the duty of a physician to give her the proper advice to safeguard her. There is no moral obligation which compels a married woman to have an unlimited number of children, or, as a matter of fact, any children at all. Conditions may arise in the life of a married couple which may make childbearing inadvisable or even morally wrong. I am, therefore, in accord with the general principles in Dr. Toland's paper. I am, however, unalterably opposed to his applications of these principles and his recommendations.

He fails to present any data in Groups I and II on which a decision could be reached, except to mention casually the diseases that the patients suffered. I will not take issue with him on these first two groups. They might or might not present difficulties. I do take serious issue with him on his third and largest group. I have read and reread that part of his paper referring to this group of 369 patients, hoping that I might find some bit of information that would justify him in his conclusions and recommendations. He frankly admits that the records on which his conclusions are based are inadequate.

He tells us nothing of the patients' early history, nothing of their state of health or their economic status, nothing of their individual desire for children; in fact, nothing except that without any knowledge other than that his patients have had from two to five children, he is to be the judge as to how large the family should be.

Let us forget all ethical considerations in this discussion and limit it to several phases on which we can meet on a common ground. I have been against the Birth Control Movement since its inception and I would be against it if I were an Atheist. No matter how clean and commendable the motives of the instigators of this movement might have been, any thinking person must see that they have unleashed forces which both destroy the morality of our people and threaten the very life of the nation.

Let us look at this question from another angle. Dublin, who is perhaps the greatest authority on population, states: "Remarkable changes are taking place in the population of the United States. Few of those in high places realize how far-reaching these changes are. How many know that the present generation is not reproducing itself?" "It is high time that those responsible for our future planning take into consideration the matter of our population rather than those grandiose promises which they will never fulfill. The present rate of decline in births cannot continue without the disastrous consequences of early race suicide."

In 1906, when the population of Pennsylvania was approximately seven million, there were 167,000 births per year. In 1932, when the population had increased to ten million, the birth rate in Pennsylvania was 168,000 a year. During a ten-year period from 1921, the American birth rate dropped 17 per cent; Connecticut 34.9 per cent; New Jersey 34.5 per cent. New Mexico and Arizona had the only normal increase in birth rate.

I have never had a quarrel with birth control where it is legitimately used. I have always maintained that in the final analysis, it is a purely medical problem and should be limited to members of the medical profession.

DR. JOHN M. FISHER.—During a period of ten years in Pennsylvania, Connecticut, and New Jersey there has been an average decline in the birth rate of 32.8 per cent. In the July *Scribner's* Spangler states that we are approaching the time when there will be an annual shortage of half a million births in the United States. Even now in northern and western Europe there is an annual deficit of ten million births.

Reliable statistics indicate that the population of a nation can be kept at its accustomed level only when an average of from three to four children are born to each family. This proportion in our country is not maintained. That which is most lamentable, however, is that the older, well-established families are diminishing in numbers in ever increasing proportion.

By the adoption of the one- and two-child system among our better stock, the hereditary transmission of potentials above high-grade morons is decreasing and the inborn intelligence level of the population in general, therefore, will continue to fall with a corresponding deterioration in every department of social life and governmental administration.

In the aggregate, indiscriminate conception restriction as practiced among civilians today is vastly more destructive of our human breeds of quality than occasional wars.

In accordance with the processes of nature, the female's main duty always has been and always will be the family. In the present population dilemma this may involve national and social readjustments, and, above all, increasing responsibilities and personal sacrifices, and even some suffering, but they must be met to avoid biologic decay of the race.

All women of good quality must be made to know and feel that marriage and children and the exercise of their inborn capacities for creating homes that are uplifting and durable, lead to the highest ideals of racial development and good citizenship. Birth selection rather than birth control is the best available means

for securing human improvement. Those who defy evolutionary processes by the popularization and practice of indiscriminate birth control are wielding a two-edged sword that eliminates both the fit and the unfit.

If the people of our Western civilization are to approach stability of a population of quality, rise in power individually and collectively, it becomes the first and primary function of women of quality to marry good biologic stock and bear three to four or more children.

If society is so constituted that it offers barriers to such a consummation, then it must be reorganized to meet existing demands or suffer the inescapable consequences.

DR. B. C. HIRST.—I have studied this matter quite intensively in the past two or three months. Entering this study with an entirely unprejudiced mind, I agree with Dr. McGlinn. There is real cause for alarm for the future of the country.

An estimate of barren marriages in this country was in 1914, 13 per cent and in 1928, 17 per cent. In 1910 the size of the average American family was found to be 3.67; in 1920, 3.58, and in 1930, 3.57. The marriage rate in this country in 1931 was the lowest ever reported in the United States.

A serious matter is the contrast in the birth rate of the United States generally with that of Mississippi, West Virginia, Alabama, North and South Carolina. Due to the Negroes these states have a birth rate of 23.8 compared with an average of 18 per thousand in the United States. The upper classes are not reproducing; the lower classes are more than reproducing themselves. These conditions cannot continue without deterioration of the population.

Dr. Schumann spoke of overpopulation. Belgium has a population of 680 to the square mile, ours is 41.3. We might multiply ten times and yet have only three-fourths of the condensation of population in Belgium.

DR. CLIFFORD B. LULL.—I believe, as a member of the Lying-In Hospital Staff, that it should be very definitely emphasized that these cases quoted by Dr. Toland in his statistics have not been given contraceptive advice at the hospital. They were selected from our case records as, in his opinion, entitled to be given contraceptive advice.

DR. EDWARD A. SCHUMANN.—There is an argument of weight which is opposed to Dr. Hirst's reasoning. First, it has never been shown that mere increase in population leads to any particular excellence of the population. Also, the reason that has led men to insist upon large families is based upon the selfish attitude of State and Church that men mean soldiers. The more rapidly this viewpoint is altered, the better for future civilization. In the past agricultural age, children were an asset and not a liability. The man who had twelve sturdy sons to help in tilling the fields was infinitely better off than he who had but one or two. But since the development of the machine there is no necessity whatsoever for these excessive families. Dr. Hirst made a very significant statement when he spoke of the increase in population of the southern states which I think is a very strong argument for the spreading of birth control, rather than for its suppression. Generally speaking, what is the object of having an increased population when the country is not able to care for its present inhabitants, and in the last analysis, what is the advantage in mere numbers?

DR. N. W. VAUX.—I think that Dr. Toland's paper may have been misunderstood. We all agree that there are certain patients who need protection against a pregnancy which may be life-threatening to the individual, and I do not think any doctor will question that fact.

There are certain cases which need contraceptive care and advice, and at the present time the state of Pennsylvania prevents any contraceptive instruction being given. A body like this should take a strong stand in the matter to have this existing law changed.

DR. PHILIP F. WILLIAMS.—Several years ago, a member of the Milbank Foundation visited Philadelphia for the purpose of investigating through the hospitals of this city the extent and results of birth control practice. A comparative statement was given out by the agent of the Foundation concerning the investigation of women who had, and women who had not, used contraceptives. Of those who had not, a large proportion had become pregnant within two years after the birth of their last child, and of those who had used contraceptives, practically the same proportion had become pregnant within two years after the birth of their last child!

Now it seems that if there was a perfectly safe birth control system then it might be advised under certain restrictions, and women be allowed the choice of using it. But when such methods are so unreliable, I think we should turn to another solution for women who become pregnant when they should not, or do not want to. I refer to legalized abortion. I believe we have been very narrow-minded in this country on this subject, and I believe the present situation gives us a good opportunity for widening this method of legalized abortion in hospitals. Those who have seen the statistics of preventable deaths in Pennsylvania realize the enormousness of this problem in this city where deaths from sepsis due to induced or criminal abortion outnumber the deaths from sepsis at term. Possibly instead of discussing birth control measures, we might turn profitably to a discussion of broadening the indications for therapeutic abortions.

DR. JOHN M. LAFERTY.—The present morbid interest of various uplift organizations in the subject of contraception has been instigated largely by profit-seeking reformers and their sentimental or pathologically minded dupes. It is an old subject and was probably an old subject in the time of Onan. On this question, as on prohibition, prison reform, eugenics, euthanasia, and kindred topics, the physicians, by expressing professionally pseudoauthoritative opinions, merely make medicine ridiculous. It is no wonder, after being taught the asinine account of the evil effects of alcohol and tobacco on the bones, and reading the conflicting and foolish testimony of many neurologists in legal cases, and hearing of the erotic shows conducted behind the closed doors of medical societies, laity begins to lose respect for the physician.

Most patients suffering from serious illness are either sterile or abort, or suffer from loss of libido. In such conditions as tuberculosis, heart disease, and chronic nephritis, it is debatable if the disease is made much worse by pregnancy when proper prenatal care is given.

Much harm can be done by advising patients against pregnancy, and morbid lives and broken homes have resulted from such thoughtless advice given by physicians without adequate reason.

DR. TOLAND (concluding).—Dr. Hirst has, I feel, already been well answered by Dr. Schumann, but I would like to add that, while I think that Dr. Hirst's reasoning is excellent as far as it goes, he did not carry it far enough. The intelligentsia, and by that I do not mean sophisticated novel readers, but the intelligent men and women we come in daily contact with, are unquestionably practicing birth control; and regardless of what the medical profession does or says, they will continue to do so, and have their children when, as, and if they want them, and not haphazard. The only way to equalize the differential in birth rate now existing between the masses and the classes, is to take a humanitarian and eugenic point of view, and see to it that we spread contraceptive information, when needed, to the

strata who are not intelligent enough to dig it out for themselves. This can only be properly done by the cooperation of the medical profession.

In answering Dr. McGlinn I would like to say that I am much more in accord with him than he thinks. I am quite in favor of taking this matter out of the hands of the laity, particularly the birth control societies whose activities he decries. It is perfectly obvious that we are discharging women every day from our hospitals who need contraceptive advice urgently. What do we do about it? Nothing whatever! The result is that at present most contraceptive information is bootlegged by drug clerks, midwives, and lay friends; the methods advocated are usually unreliable and often harmful. The truth is that the laity have gotten a step ahead of our profession in the matter of contraception. Intelligent people, impatient at our slowness to grasp this opportunity to aid our maternity patients, have countenanced and encouraged the activities of the birth control societies. I think it is high time the medical profession recaptures the lead in this branch of preventive medicine which rightfully belongs to it.

THE INCIDENCE, TREATMENT, AND MORTALITY OF ECLAMPSIA*

Analysis of 123 Cases

Joseph Binder, M.D., Jersey City, N. J.

(From the Obstetric Department of the Jersey City Medical Center and the Margaret Hague Maternity Hospital)

WHILE this presentation will not contribute anything new to the subject of eclampsia, it will demonstrate that the incidence of eclampsia is lowered by prenatal care and early hospitalization; that the conservative treatment of eclampsia has a wider field of usefulness than the radical treatment, and it will very definitely reduce maternal and fetal mortality.

This study is based on 13,354 patients discharged, from July 1, 1926, to Oct. 19, 1932, in which there were 123 cases of eclampsia.

Adequate prenatal care is synonymous with prophylactic treatment and is our most formidable weapon in eclampsia. The incidence will be reduced if our hospitals are more willing to accept for treatment and observation potentially or truly toxemic patients and if physicians in practice recognize the potential dangers of rapid gain in weight, rise in blood pressure, edema, epigastric distress, visual disturbances and headaches, and hospitalize these patients at once.

We have noted that with the increased facilities for earlier hospitalization of our toxemic or potentially toxemic patients, our eclampsia incidence was in inverse ratio to our toxemic admissions incidence. Thus from 1926 to 1932, our toxemia admission incidence increased from 1:29 to 1:17 and our eclampsia incidence decreased from 1:74 to 1:154.

---

*Read, by invitation, before the Obstetric Section, New York Academy of Medicine, December 27, 1932.

TABLE I

		ECLAMPSIA	INCIDENCE
Incidence of Eclampsia			
Radical Period: J. C. Hospital July, 1926—Dec. 31, 1928			
Cases discharged	3320	45	1:74
Conservative Period: J. C. Hospital 1929—Oct. 15, 1931			
Cases discharged	5399	48	1:113
Conservative Period: M. H. M. Hospital Oct. 16, 1931—Oct. 19, 1932			
Cases discharged	4635	30	1:154
Total	13354	123	Average 1:109

Incidence of Toxemia

	TOXEMIA	INCIDENCE
1926—1928		
3320	113	1:29
1929—Oct., 1931		
5399	261	1:21
Oct., 1931—Oct., 1932		
4635	266	1:17

Preeclampsia is so closely allied to eclampsia that it can well be considered eclampsia without convulsions. It is this condition which, if recognized and treated early, will prevent convulsions or coma in nearly all cases.

It is hardly conceivable that with our present lack of knowledge of the etiology of the disease, eclampsia can be wholly prevented in spite of the most careful prenatal observation, because we have seen patients with adequate prenatal care and an uneventful pregnancy, without any warning, seized with eclamptic attacks. Yet this very occasional occurrence should not discourage us.

Of 10,188 patients that had prenatal care there was an incidence of 1:196, while in 3166 unobserved cases it was 1:45.

Most of our severest forms of eclampsia have occurred in the nonclinic case. It was not uncommon for these to have five or more convulsions.

Since 1928 there has been an increase in the number of mild postpartum eclampsias. The majority of these had one or two convulsions, which were very promptly controlled by the treatment at present in vogue.

Prenatal care has, in our experience, resulted in a very definite decrease in incidence; a definitely milder type of eclampsia when it occurred, and is unquestionably an important factor in the decrease of maternal and fetal mortality. As Bill of Cleveland has said, "It has become an inseparable part of the treatment of eclampsia."

From the many theories of eclampsia there have evolved as many different types of treatment, and the type chosen will depend upon the theory that appeals most to one's imagination and to one's personal experience.

In the past fifteen years, there has been a considerable change in the treatment of eclampsia. Preceding this period, it was almost universally felt that inasmuch as only the pregnant woman had eclamptic convulsions, her pregnancy, which was the responsible factor, should be terminated. Hence, accouchement forcé, vaginal cesarean sections, high forceps, version or abdominal section under general anesthesia was current practice and exacted a high *fetal and maternal* toll; the fetus succumbing to trauma, toxemia or prematurity, and the mother to eclampsia per se or very frequently to shock, hemorrhage and infection.

Our treatment during the past fifteen years represents the trend of changes in the treatment of eclampsia.

During the period 1915 to 1920, on admission, the patient was given morphine in repeated doses until the respirations were 8; veratrum viride until pulse was below 90; two ounces of saturated solution of magnesium sulphate or croton oil Mii after gastric lavage. As we were definitely committed to an active policy, the patient was prepared for delivery as soon after admission as was possible. Many of them were sectioned, others had labor started or hastened by bagging, vaginal section, forceps, or version.

In the early part of 1920, we abandoned the use of veratrum viride and croton oil.

To aid elimination, gastric lavage, high colonic irrigations and wet and later dry hot packs were used. In addition, we employed the intravenous administration of Hogan's gelatin solution and occasionally we resorted to phlebotomy. The anesthetics then in use were ether, gas, oxygen, ether and local infiltration.

From 1920 to 1925, our treatment was still active. We practiced immediate or early emptying of the uterus by the method that was least exhausting or traumatic to the patient. After delivery, control of the convulsions was attempted by the use of morphine; choral and bromides per rectum; paraldehyde; elimination by gastric lavage, high colonic irrigation and hot packs.

Following Lazard's[2] lead, we instituted the use of magnesium sulphate 10 per cent intravenously and intramuscularly. Shortly after Thalheimer's[3] first paper we incorporated in our treatment, the intravenous administration of 1000 c.c. of glucose 5 to 10 per cent with insulin 15 to 25 units. Phlebotomy was still occasionally done and this was frequently followed by blood transfusion. We felt at that time that the patients recovered from their coma much earlier and that the glucose and insulin were probably responsible for this.

In 1926, with this treatment as adjuvant to our active treatment, we felt that our maternal and fetal mortality would be as low as that claimed by the conservative school.

For the sake of comparison, we have divided our treatment during 1926 to 1932 into three phases:

1. July, 1926 to Dec. 31, 1928—representing our radical phase of treatment.
2. Jan., 1929 to Oct. 15, 1931—representing our conservative phase of treatment at the Jersey City Medical Center.
3. Oct. 16, 1931 to Oct. 19, 1932—representing continuation of treatment (conservative) at the Margaret Hague Maternity Hospital.

First or Radical Phase at the Jersey City Medical Center.—Our routine treatment during the radical phase, 1926 to 1928, was as follows: immediately on admission, the patient was isolated; morphine gr. ¼, and 20 c.c. of 10 per cent magnesium sulphate was given intravenously and repeated every hour until the convulsions were controlled. One hour after admission, an intravenous injection of 1000 c.c. of glucose was given, 5 to 10 per cent, with 15 to 25 units of insulin; the next hour a high colonic irrigation of 5 per cent sodium bicarbonate; and for continued restlessness, bromides and chloral per rectum, every four hours.

If there was no apparent response in a few hours, labor was hastened or pregnancy terminated, the time and type of procedure depending upon the condition of the patient, the size and viability of the child, the age and parity of the patient, the condition of the cervix and the size of the pelvis.

Since many European and American obstetricians continued to report excellent results with the conservative method of treatment, it was decided early in 1928 to try this. A survey of the results of our treatment during the two and a half years ending 1928, showed that there was a very definite improvement in maternal mortality in that part of 1928 during which conservatism was practiced.

Second Period, Conservative Phase at Jersey City Medical Center.—Beginning January, 1929, therefore, all eclampsias were treated conservatively. We selected from our personal experience and from the literature on eclampsia those features which best answered the requirements and purposes of conservative treatment.

First: To lessen irritability of the nervous system; lower blood pressure; lessen intracranial pressure and thereby control or prevent recurrence of convulsions or coma.

Second: To promote elimination or decrease toxin concentration.

To lessen irritability of the nervous system; lower blood pressure; lessen intracranial pressure and to control or prevent the recurrence of convulsions or coma.—

1. The patient was placed in a darkened room, isolated from other patients or noises. Attendants were instructed to avoid all unnecessary manipulations or examinations. No active restraint was practiced on the unruly or restless patient. She was prevented from throwing herself out of bed by being placed in a specially constructed bed resembling a baby crib. Care was taken to prevent injury to the tongue.

2. Twenty cubic centimeters of 10 per cent solution of magnesium sulphate was immediately administered intravenously and was repeated every hour until the convulsions were controlled, after which the frequency of administration was decreased.

3. Morphine sulphate gr. ¼ was given and rarely repeated.

4. Bromides gr. xl-lx in combination with chloral hydrate gr. xx-xxx were administered per rectum every four to six hours to maintain sedation.

To promote elimination and decrease toxin concentration.—

1. Hypertonic solution of glucose, 300 c.c. of 25 per cent was given very slowly

according to the method of Titus, i.e., at the rate of 4 c.c. per minute. It was repeated at intervals of four to twelve hours depending upon the severity of the case and the response to treatment. In addition 1000 c.c. of 10 per cent glucose was occasionally given. *No insulin* was used.

2. High colonic irrigations of 5 per cent sodium bicarbonate were given at twelve-hour intervals to aid intestinal elimination.

3. To aid aspiration and drainage of fluids from the trachea in the presence of pulmonary edema, the patient was put on her side with the head low and the catheter or suction tube used.

4. Venesection was occasionally resorted to in threatening right heart failure.

5. As soon as the patient was conscious and could swallow, fluids, fruit juices, well sweetened, were given in small amounts and then gradually a high carbohydrate diet, low in protein and salt-free.

Since the majority of antepartum eclamptics began labor shortly after the onset of convulsions, no effort was made to hasten the onset of labor. Wherever possible, the second stage was expedited by low forceps and episiotomy under spinal anesthesia.

During this conservative phase at the Jersey City Medical Center, Jan. 1, 1929, to Oct. 15, 1931, two antepartum eclampsias in the seventh month of gestation, responded to treatment and were discharged well of their eclampsia. Both subsequently delivered without recurrence of their eclampsia.

Third Period, Conservative Treatment, Margaret Hague Maternity Hospital, 1931 to 1932.—This same policy of conservatism has been practiced at the Margaret Hague Maternity Hospital and the details of treatment are essentially the same except for minor variations, such as the frequent substitution of magnesium sulphate 3ii daily for mild catharsis instead of the routine high colonic irrigations; and the occasional intravenous injection of 50 c.c. of 50 per cent solution of glucose, in an effort to obtain better cerebral dehydration.

Analysis of Results of Treatment.—During the radical phase, there were 45 eclampsias in 3320 patients, an incidence of 1:74. Our maternal mortality was 8 or 17.7 per cent and our gross fetal mortality 44.3 per cent with 34 per cent stillbirths and 10.3 per cent neonatal deaths.

TABLE II. TYPES OF DELIVERY IN 45 ECLAMPSIAS, JERSEY CITY HOSPITAL DURING RADICAL PERIOD, JULY 1, 1926 TO DEC. 31, 1928

	SPONTANEOUS	CESAREAN	FORCEPS	VERSION	BREECH	BAG	UNDELIVERED
19 Antepartum	7a*	6b	2h	2c	1c	2ac	1x
17 Intrapartum	4	3	10h	0	0	1	0
9 Postpartum	9	0	0	0	0	0	0
45 Total	20	9	12	2	1	3	1

*a, includes one bag and spontaneous delivery.
b, includes 1 vaginal cesarean section.
h, expedite second stage.
c, bag version and breech delivery.
x, died.

Inasmuch as most of our cases of antepartum and intrapartum eclampsias occurred in primigravidas, 9 cesarean sections were performed. Four of them were done under local infiltration and the rest under spinal anesthesia with the exception of one which was done under G.O.E.

All of our forceps, except four done under G.O.E., were performed under spinal anesthesia.

Of 5399 cases discharged during the conservative period of 1929 to the closing of the Obstetric Department at the Jersey City Medical Center, Oct. 15, 1931, there were 48 eclampsias, an incidence of 1:113, with only 4 deaths or a maternal mortality of 8.3 per cent. Two of these deaths occurred one-half to one hour after admission, a corrected mortality of 4.1 per cent. Our fetal mortality was 30.6 per cent of which 20.4 per cent were stillbirths and 10.2 per cent neonatal deaths.

Not one cesarean section was done for eclampsia per se. One antepartum case was sectioned for mechanical indications. Two cases that were sectioned because of contracted pelvis developed postpartum eclampsia several hours after delivery. Four other patients also developed convulsions, postpartum, following low forceps delivery for outlet arrest.

TABLE III. TYPES OF DELIVERY IN 48 ECLAMPSIAS, JERSEY CITY HOSPITAL DURING CONSERVATIVE PERIOD, JAN. 1, 1929 TO OCT. 15, 1931

	SPONTANEOUS	CESAREAN	FORCEPS	VERSION	BREECH	BAG	UNDELIVERED
13 Antepartum	6	1a*	2h	2m, tr	1tr	2m, n	2c
16 Intrapartum	4	0	8h	1t	1	0	2d
19 Postpartum	12	2b	4h	0	0	1l	0
48 Total	22	3	14	3	2	3	4

*h, expedite second stage.
a, b, for contracted pelvis.
m, antepartum eclampsia, bagged, died p.m., version.
n, threatened recurrence of eclampsia.
c, discharge.
t, twin.
tr, triplet.
l, toxic patient who developed postpartum eclampsia.
d, died one-half and one hour after admission.

IN 30 ECLAMPSIAS, MARGARET HAGUE MATERNITY HOSPITAL DURING CONSERVATIVE PERIOD, OCT. 15, 1931 TO OCT. 19, 1932

	SPONTANEOUS	CESAREAN	FORCEPS	VERSION	BREECH	BAG	UNDELIVERED
7 Antepartum	4b	0	1h	0	1a	2a, b	0
6 Intrapartum	1	0	5h	0	0	0	0
17 Postpartum	6d	1k	9h, e	1d	1e	0	0
30 Total	11	1	15	1	2	2	0

*a, bagged, breech delivery.
b, 1 bagged, spontaneous delivery.
c, twin, 1 forcep and 1 breech.
d, twin, 1 spontaneous and 1 version.
k, operated for sterilization because of repeated toxemia. Developed postpartum eclampsia four days later.
h, expedite second stage.

There were two versions and two breech extractions in a triplet and twin pregnancy. One version was done postmortem on a patient who died intrapartum.

During our first year, Oct. 16, 1931, to Oct. 19, 1932, at the Margaret Hague Maternity Hospital, there were 4635 patients discharged in whom 30 cases of eclampsia occurred, an incidence of 1:154 with 2

TABLE IV. FETAL MORTALITY

	STILL-BIRTHS	LIVING	NEONATAL DEATHS	DISCHARGED LIVING
Radical Period—J. C. H.				
July, 1926 to Dec. 31, 1928				
Number	15	28	3	26
Per cent	34%	66%	10.3%	*56%*
Conservative Period—J. C. H.				
Jan. 1, 1929 to Oct. 15, 1931				
Number	10	39	5	34
Per cent	20.4%	79.6%	10.2%	*69.8%*
Conservative Period—M. H. M. H.				
Oct. 16, 1931 to Oct. 19, 1932				
Number	6	26	1	25
Per cent	19%	81%	4%	*77%*

TABLE V. ANESTHESIA

	LOCAL	SPINAL	G. O. E.	AVERTIN	ETHER
1926 to 1928	4	16	5	0	0
1929 to 10/15/1931	0	21	0	1	0
10/16/1931 to 10/19/1932	1	14	1	0	4

NOTE: All the local anesthesias were for cesarean sections. All ethers were for cases that eventually developed postpartum eclampsia. All G. O. E. anesthesias were for cesarean sections with the exception of one done in 1932 for low forceps in intrapartum eclampsia.

TABLE VI. STATISTICAL STUDY OF 123 CASES OF ECLAMPSIA JULY 1, 1926 TO OCT. 19, 1932*

	ANTEPARTUM	INTRAPARTUM	POSTPARTUM	TOTAL
Radical Period, July 1, 1926, to Dec. 31, 1928, Jersey City Hospital, Department of Obstetrics				
No.	19	17	9	45
Deaths	4	2	2	8
Per cent	21	11.6	22.2	*17.7*
Conservative Period, Jan. 1, 1929 to Oct. 15, 1931, Closing of Department of Obstetrics, Jersey City Hospital				
No.	13	16	19	48
Deaths	1	2	1	4
Per cent	7.6	12.5	5.2	*8.3*
Conservative Period Continued at Margaret Hague Maternity Hospital, Oct. 16, 1931 to Oct. 19, 1932				
No.	7	6	17	30
Deaths	0	1	1	2
Per cent	0	16.6	5.9	*6.6*

*NOTE: During radical period July 1, 1926 to Dec. 31, 1928. 45 cases, mortality 17.7 per cent. During conservative period Jan. 1, 1929 to Oct. 19, 1932, a total of 78, mortality 7.7 per cent.

52 Clinic cases, 3 deaths, 5.8 per cent mortality.

71 Nonclinic cases, 11 deaths, 15.3 per cent mortality.

deaths or a maternal mortality of 6.6 per cent and a gross fetal mortality of 23 per cent with 19 per cent stillbirths and 4 per cent neonatal deaths. No cesarean sections were done for eclampsia. One cesarean section was done for severe toxemia and the patient developed postpartum convulsions four days later and died.

Our mortality in 45 cases with the former type of treatment (1926-1928) was 8 or 17.7 per cent. Of these there were 36 antepartum and intrapartum cases with a mortality of 16.6 per cent.

During the conservative phase of treatment (1929-1932) in 78 cases, there was a mortality of 6 or 7.7 per cent. Of these there were 42 antepartum and intrapartum cases with a mortality of 4 or 9.5 per cent.

In 52 eclampsias that had prenatal care there were 3 deaths or 5.8 per cent. In 71 eclampsias that had no prenatal care there were 11 deaths or 15.3 per cent.

CONCLUSIONS

1. Prenatal care, early recognition of toxemia, and early hospitalization has decreased the incidence of eclampsia from 1:74 to 1:154.

2. There were 3 deaths or 5.8 per cent mortality in 52 patients that had attended our clinic compared to 11 deaths or 15.3 per cent mortality in 71 cases that had not attended clinic.

3. An analysis of the radical and conservative phases of treatment demonstrated that the conservative treatment gave us the best results, to wit:

a. There was a marked decrease in maternal mortality from 17.7 per cent to 7.7 per cent.

b. The gross fetal mortality was reduced from 44.3 per cent to 27.1 per cent.

4. Cesarean section in the eclamptic should be reserved for pelvic indications.

5. Low forceps and episiotomy to expedite the second stage of labor did not increase our mortality.

6. Spinal anesthesia is the anesthesia of choice.

I wish to take this opportunity of thanking Drs. Cosgrove, Waters, and Norton for the privilege of including cases from their services in this analysis.

REFERENCES

(1) *Bill, A. H.:* Am. J. Obst. & Gynec. **23**: 155, 1932. (2) *Lazard, E. M.:* Am. J. Obst. & Gynec. **9**: 178, 1925. (3) *Thalheimer, W.:* J. A. M. A. **82**: 696, 1924.

422 Bergen Avenue.

A POSSIBLE DERIVATION OF GUANIDINE AND HISTAMINE IN THE AUTOLYSIS OF ACUTE PLACENTAL INFARCTS AND THEIR PROBABLE RELATION TO ECLAMPTIC TOXEMIA

R. A. Bartholomew, M.D., and Francis Parker, M.D., Atlanta, Ga.

IN A RECENT publication,[1] clinical, pathologic and experimental evidence was given, supporting the view that eclamptic toxemia is due to poisonous split products of placental protein, particularly guanidine and histamine, produced during the autolysis of acute placental infarcts. A diagrammatic representation summarizing a part of this evidence is herewith presented, together with a discussion of

DIAGRAMATIC REPRESENTATION OF PROBABLE RELATION OF PLACENTAL INFARCTS TO PRE-ECLAMPSIA, ECLAMPSIA AND ABRUPTIO PLACENTAE

PROBABLE ETIOLOGY	PHYSIOLOGIC ENDARTERITIS SLOW OCCLUSION	TRAUMA OF FETAL MOVEMENTS ON PLACENTAL VESSELS CAUSING RUPTURE, THROMBOSIS OR EMBOLISM.	TRAUMA OF FETAL MOVEMENTS ON PLACENTAL VESSELS CAUSING RUPTURE, THROMBOSIS OR EMBOLISM.
COURSE	SLOW 1-3 MONTHS	ACUTE OR SUBACUTE 1-3 WEEKS	ACUTE OR SUBACUTE 1-3 WEEKS
LOCATION	USUALLY ON OR NEAR MARGIN ON MATERNAL SURFACE.	USUALLY IN INTERMEDIATE OR CENTRAL ZONE IN SUBSTANCE.	USUALLY IN INTERMEDIATE OR CENTRAL ZONE ON MATERNAL SURFACE
GROSS APPEARANCE	WHITE OR YELLOW-WHITE	DARK, CONGESTED, PURPLE OR BROWN	DARK, CONGESTED OR BROWN-RED
CONSISTENCY	FIRM	SOFT TO SLIGHTLY FIRM	SOFT TO SLIGHTLY FIRM
MICROSCOPIC APPEARANCE	NECROTIC "GHOST" VILLI, WITH SURROUNDING HYALINE INTERVILLOUS SUBSTANCE OR HYALINE VILLI WITH OPEN INTERVILLOUS SPACES.	NECROTIC VILLI, MARKED DILATATION AND CONGESTION OF CAPILLARIES OF VILLI, SOME RUPTURED OR THROMBOSED. OPEN INTERVILLOUS CIRCULATION.	NECROTIC VILLI, MARKED DILATATION OF CAPILLARIES OF VILLI, SOME RUPTURED OR THROMBOSED. OPEN INTERVILLOUS CIRCULATION, MORE EVIDENCE OF HEMORRHAGE
BIOCHEMISTRY	SLOW AUTOLYSIS POISONING PREVENTED BY SLOW HYALINE CHANGE OR BY THE FORMATION OF HYALINE INTERVILLOUS SUBSTANCE PREVENTING ABSORPTION.	RAPID AUTOLYSIS PROBABLE INHIBITION OF COAGULATION OF MATERNAL BLOOD BY PEPTONE SUBSTANCE, HENCE FREE INTERVILLOUS CIRCULATION AND ABSORPTION OF PEPTONE, GUANIDINE AND HISTAMINE.	RAPID AUTOLYSIS CONCENTRATION OF PEPTONE, GUANIDINE AND HISTAMINE ON LOCALIZED AREA. HISTAMINE CAUSES RUPTURE OF ADJACENT DECIDUAL SINUSES AND EXTRAVASATION OF MATERNAL BLOOD.
CLINICAL EFFECT	NO TOXEMIA	GUANIDINE ACTION PROBABLY PREDOMINATES. PRE-ECLAMPSIA AND ECLAMPSIA	HISTAMINE ACTION PROBABLY PREDOMINATES. ABRUPTIO PLACENTAE BEFORE ECLAMPSIA CAN DEVELOP.

Fig. 1.

the possible derivation of guanidine and histamine, in the course of autolysis of acute placental infarcts and their probable relation to eclamptic toxemia.

According to Harding and Fort,[2] analysis of placental tissue showed the following nitrogen distribution: Amid 6.34 per cent; humin 3.20 per cent; arginine 24.08 per cent; histidine 2.32 per cent; lysine 7.34 per cent; and cystine 1.47 per cent. They call attention to the strikingly high content of arginine in the placenta, which is about twice that of any other tissue.

The arginine, which normally is derived from protein digestion in the intestinal tract, is carried by way of the mesenteric and portal veins to the liver, where a special enzyme, arginase, found mainly in the liver and kidney, breaks it up into urea and ornithine.

If, however, acute infarction occurs in the placenta, the absence of the special enzyme arginase, may possibly allow the decomposition of arginine to begin at the carboxyl end of the chain and finally liberate guanidine by an oxidation process, according to the following oxidation reduction reactions, in which CO_2 and H_2O are given off with each step:

POSSIBLE FORMATION OF GUANIDINE FROM ARGININE BY OXIDATION REDUCTION

Arginine (Guanidine alpha amino-valerianic acid)

$$NH_2 - C(=NH) - NH - CH_2 - CH_2 - CH_2 - CH(NH_2) - COOH \rightarrow$$

Guanidine alpha oxy-valerianic acid

$$NH_2 - C(=NH) - NH - CH_2 - CH_2 - CH_2 - C(=O) - COOH + \uparrow NH_2 \rightarrow$$

Guanidine butyric acid

$$NH_2 - C(=NH) - NH - CH_2 - CH_2 - CH_2 - COOH \rightarrow$$

Guanidine proprionic acid

$$NH_2 - C(=NH) - NH - CH_2 - CH_2 - COOH \rightarrow$$

Guanidine acetic acid

$$NH_2 - C(=NH) - NH - CH_2 - COOH \rightarrow$$

Guanidine formic acid

$$NH_2 - C(=NH) - NH - COOH \rightarrow$$

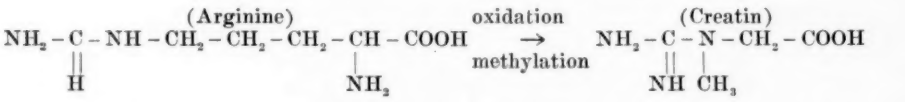
Guanidine

$$NH_2 - C(=NH) - NH_2$$

The above reactions may possibly take place under the influence of oxidases and reductases which are present in the tissues. The deaminization reaction may take place by oxidation in a manner similar to the transformation of alanine to pyruvic acid as set forth by Dakin.[3]

$$\underset{\text{(alanine)}}{CH_3 - CH(NH_2) - COOH} \quad \underset{\text{(oxidation)}}{\rightarrow} \quad \underset{\text{(pyruvic acid)}}{CH_3 - C(=O) - COOH}$$

Knoop's theory of beta oxidation, so strictly adhered to in the past, is no longer thought to be the only mechanism of oxidation of straight chain carbon compounds. Under some conditions, the oxidation of the chain takes place one carbon at a time. This is necessary to account for the formation of creatin from arginine:



Beta oxidation would leave either a one or a three carbon chain on the guanidine group. There is also the possibility that both types of oxidation take place in the same compound.

The variations in the P_H of the tissues involved cannot be overlooked as an important factor influencing the type of reaction which may take place. Large infarcts are acid in reaction, while small infarcts are alkaline, due, possibly, to the neutralizing effect of the surrounding alkaline (P_H 7.3 to 7.4) tissue fluids.[4] In small infarcts this fluid is able to penetrate the whole infarcted area and neutralize any tendency to acidity, while in the center of large infarcts there is a marked acid reaction with a gradual transition to alkalinity toward the periphery. It is strongly probable that this condition influences the type of enzyme action. Arginase acts best in an alkaline medium (P_H 10)[5] or in neutral medium (P_H 7.0)[16] hence its action should be greatly inhibited by acidity. On the other hand, the protease found active in autolyzing animal tissue has its optimum action at a P_H 4.5.[6] Such condition should inhibit the formation of urea and ornithine from arginine and promote oxidation of the carbon chain to guanidine. In the absence of bacterial putrefaction, deaminization in amino acids would begin with the alpha amino group, and the amid group, such as is in guanidine, would not be affected. Such action would probably preserve the guanidine group intact after the carbon chain had been removed by oxidation.

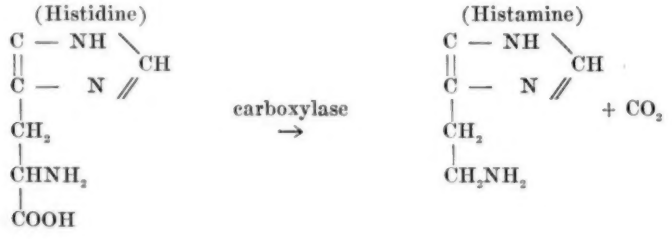
The formation of guanidine from creatin as advanced by Titus, et al.[7] differs only slightly from the above. However, their work leads one to believe that guanidine is possibly formed from the creatin normally present in the tissues, and not that there is an abnormal chemical reaction taking place beginning with arginine and possibly not passing through the stage of creatin formation.

It is much less probable that arginine may be formed from histidine in vivo or that guanidine may result from the nucleoproteins by way of guanine.

Histamine, a decarboxylation product of histidine, is normally formed in the large intestine by the action of the colon group of bacteria specific for histidine. Mitchell and Hamilton[8] state that the occurrence of histamine as a product of proteolysis seems improb-

able as its presence has never been noted in protein hydrolysates. Abel and Kubota[9] offered rather unsatisfactory evidence for its presence, and the same work repeated by Hanke and Koessler in 1920, gave negative results. However, Best, et al.[10] in 1927, isolated relatively large amounts of histamine from several animal tissues, and Thorpe[11] in 1928 isolated it from muscle.

Liver and muscle under sterile conditions, have the capacity of decarboxylating pyruvic acid, possibly by action of a carboxylase.[12] A similar capacity for destroying pyruvic acid has also been found in human placenta.[13] Unless the carboxylase present is specific for pyruvic acid, it is quite possible that histidine may be transformed into histamine by decarboxylation within the cell, as in the following equation:



The outstanding effects of guanidine poisoning, as summarized by Titus, et al.[7] are (1) disturbance in carbohydrate metabolism; (2) fluctuation in blood sugar (hypoglycemia); (3) increase in blood uric acid, amino acids and lactic acid; (4) increase in blood pressure; (5) edema; (6) renal damage; and (7) convulsions. Liver damage suggestive of that found in eclampsia was obtained by repeated injections of guanidine in rats.

Among the physiologic and pathologic effects of histamine may be mentioned the increase in gastric and salivary secretions; stimulation of smooth muscle, causing constriction of bronchioles, increased peristalsis, marked contraction of uterine muscle, and increased permeability of capillaries from damage to the vessel walls, which results in dilatation and rupture of small capillaries and veins, markedly lowering the blood pressure and causing shock. Peripheral necrosis of the anemic and hemorrhagic types are found in the liver[14] and associated with thrombi in the vessels. There are also degenerative lesions in the epithelium of the convoluted tubules of the kidneys.

A consideration of the physiologic and pathologic effects of injections of guanidine and histamine cannot fail to impress one with the fact that these symptoms and findings are strikingly similar to those found in preeclampsia, eclampsia, and abruptio placentae. While guanidine, histamine, and probably peptone are the chief poisons concerned, the question as to whether preeclampsia, eclampsia, or ab-

ruptio placentae will occur, probably depends on the number, size, and location of the infarcts, the degree of blockage of the circulation and the rate of autolysis.

Histamine is probably the more important factor in abruptio placentae, by reason of its damaging effects on the decidual sinuses, particularly when the autolyzing infarct is situated on the maternal surface of the placenta. This probably permits a greater concentration of histamine on a localized area, disrupting the decidual septa and sinuses and causing an extravasation of blood which soon spreads sufficiently to cause separation of the placenta. The well-known prevalence of hemorrhages throughout the uterine muscle and under the peritoneal surface of the uterus, the marked dilatation of the veins, the presence of serosanguineous fluid in the peritoneal cavity and the frequency of shock in abruptio placentae, strongly suggests the action of histamine. Abruptio placentae therefore interrupts the pregnancy before eclampsia occurs.

Guanidine is probably the more important factor in preeclampsia and eclampsia. This is strongly suggested by its action in increasing the excitability of the motor nerve endings to the constant electric current.[8] That the muscles of the preeclamptic and eclamptic patient are rendered hypersensitive in some similar way is suggested by the frequent twitchings and the ease with which convulsions are often precipitated by sudden noises or trivial disturbances. *If we grant the possible derivation of guanidine from arginine by a series of oxidation reduction reactions, it follows that the autolysis of placental tissue, which contains double the amount of arginine present in any other tissue, would probably liberate sufficient guanidine to cause convulsive seizures.* This probably accounts for the fact that while the experimental injection of a sterile autolysate of liver, kidney, or any tissue other than placenta, produces definitely poisonous effects and damage to the kidney and liver, there are no associated convulsions. Therefore the objection so frequently raised, that injection of unautolyzed placenta is without effect, or that the injection of autolyzed tissue other than placenta does not produce convulsions, is not sustained.

It is probable that in any case of toxemia of pregnancy, other than the purely nephritic type, whether it be preeclampsia, eclampsia, or abruptio placentae, the symptoms and pathologic findings are mainly those of guanidine, histamine and peptone, with such variations as may result from the rate of autolysis and the size, number and location of the infarcts. Histamine is mainly responsible for the occurrence of shock and the clinical and pathologic evidences of vascular injury, whether seen in the uterus, kidneys, liver or elsewhere in the body. Peptone also contributes to hemorrhage and shock and causes delayed coagulation time. Guanidine is the principal factor concerned

in the edema, hypertension, hypoglycemia, lowering of blood calcium and the tetany-like condition of the muscles terminating in convulsive seizures.

Finally, the therapeutic efficiency of glucose, morphine, and magnesium sulphate in eclampsia, the combination of which has been attended by a much lower maternal mortality,[15] offers additional support to the above theory. Glucose aids in dehydration, lessens edema, acts as a diuretic, minimizes liver damage, combats hypoglycemia and supports the heart. Morphine, through its nerve sedative effect, lessens the tendency to convulsions by blocking the effect of external stimuli. Magnesium sulphate, intravenously, has a curare-like effect, paralyzing the myoneural junction, thus counteracting the effect of guanidine and controlling the convulsions.

There is reason to believe that further biochemical investigation and study of the toxic products obtainable from breaking down of placental protein, may result in more specific means of recognition and neutralization and lead to the control of eclampsia.

CONCLUSIONS

1. The effects of injection of autolysate of placental tissue in animals and the close relation between the clinical evidence of toxemia and the occurrence of infarction in the placenta, strongly favor the placental theory of eclampsia.

2. The clinical and pathologic effects of guanidine, histamine, and peptone are strikingly similar to the clinical and pathologic findings in toxemia of pregnancy.

3. It is theoretically possible to obtain histamine, guanidine, and peptone from autolysis of placental infarcts.

4. Placental tissue is characterized by an unusually high content of arginine, the probable precursor of guanidine.

5. Guanidine action probably predominates in preeclampsia and eclampsia; histamine action in abruptio placentae and peptone action in certain cases of toxemia characterized by prolonged coagulation time of the blood and tendency to hemorrhage.

6. The pharmacologic action of our most reliable therapeutic agents in eclampsia, namely, glucose, morphine, and magnesium sulphate, are antagonistic to the action of guanidine and histamine.

7. If the placental theory of eclampsia is correct, it is possible that a specific means of control of the above forms of toxemia of pregnancy may be developed by biochemical investigation.

1040 PONCE DE LEON AVENUE, N. E.

REFERENCES

(1) *Bartholomew, R. A., and Kracke, R. R.:* AM. J. OBST. & GYNEC. **24**: 797, 1932. (2) *Harding, V. J., and Fort, C. A.:* J. Biol. Chem. **35**: 29, 1918. (3) *Dakin, H. D.:* Oxidations and Reductions in the Animal Body, ed. 2, London, 1922,

pp. 64-71. (4) *Gilding, H. P.:* J. Exper. Med. **52:** 953, 1930. (5) *Hunter, A., and Dauphinee, J. A.:* J. Biol. Chem. **63:** 39, 1925. (6) *Bradley, H. C.:* J. Biol. Chem. **52:** 467, 1922. (7) *Titus, P., Messer, F. C., and McClellan, R. H.:* Am. J. Obst. & Gynec. **24:** 667, 1932. (8) *Mitchell and Hamilton:* Biochemistry of the Amino Acids, Monograph Series No. 48; J. J. Little & Ives Co., N. Y., 1929, p. 370. (9) *Abel, J. J., and Kubota, S.:* J. Pharmacol. & Exper. Therap. **13:** 243, 1919. (10) *Best, Dale, Dudley, and Thorpe:* J. Physiol. **62:** 397, 1927. (11) *Thorpe:* Biochem. J. **22:** 94, 1928. (12) *Neuberg C., and Gottschalt, A.:* Biochem. Ztschr. **146:** 164, 1924. (13) *Maeda, K.:* Biochem. Ztschr. **143:** 347, 1923. (14) *Hofbauer, J.:* Am. J. Obst. & Gynec. **12:** 159, 1926. (15) *Upshaw, C. B.:* J. A. M. A. **99:** 2088, 1932. (16) *Hunter, A., and Morrell, J. A.:* Trans. Roy. Soc. Canada **16:** 75, Sec. V, 1922.

THE LENGTH OF THE HUMAN MENSTRUAL CYCLE

C. F. Fluhmann, M.D., San Francisco, Calif.

(From the Department of Obstetrics and Gynecology, Stanford University School of Medicine)

FROM time immemorial the human menstrual cycle has been considered as typically twenty-eight days in length, and any marked departure from this standard has been attributed to a pathologic condition. A careful examination of the data upon which these conceptions are based, however, leads one to entertain serious doubts as to their scientific accuracy, and the present study was undertaken in order to obtain more definite information as to the actual length of successive cycles in a series of normal women.

There is general agreement as to the length of the menstrual cycle in most of the modern textbooks and articles dealing with the problem. Schroeder[1] states that four-fifths of all normal women menstruate at twenty-eight-day intervals. Graves[2] says that the typical intermenstrual period is from twenty-seven to thirty-one days, and that there seems to be a special type of woman who menstruates every twenty-three days. DeLee[3] makes the rather startling observation that "at least 71 per cent of women menstruate every twenty-eight days, and the majority during the new moon." He also adds that there are several types, as a twenty-eight-day type, a twenty-one-day type, a twenty-seven-day type, and a thirty-day type, though some healthy women flow every six weeks. Novak[4] says that "the duration of the entire menstrual cycle, in by far the largest number of women, is twenty-eight days. A considerable number, however, menstruate regularly at intervals of twenty-one days, and a few every fourteen days. It is thus seen that the interval of days between the periods is most frequently some multiple of 7, a fact to which some significance was attached by the ancients." In a statistical analysis of 1,000 case histories, Kelly[5] found that 942 patients menstruated every twenty-eight days, but that there was "an appreciable number who did so at longer or shorter intervals." He goes on to quote a number of authors (Krieger; Hart and Barbour; Webster) who stated that the length of the cycle was of twenty-eight days in 70 to 71 per cent of cases, and of thirty days in 13.7 or 14 per cent. In an extensive study of 4,500 case histories, Sanes[6] observed that the menstrual cycle was regular in 77.5 per cent of instances, of which the twenty-eight-day type made up 72.01 per cent, while it was irregular in 22.5 per cent. Heyn[7] found that the interval was of twenty-eight days

in 63.5 per cent of 1,684 cases. An analysis of the case histories of 100 of my own private patients showed that 74 gave their menses as occurring regularly every twenty-eight or thirty days.

It would appear that these figures were based solely on the statements of patients, the majority of whom undoubtedly had made no effort to keep accurate records but simply hazarded a guess as to the probable occurrence of their menses. The scientific accuracy of such statistical analyses is open to grave doubt.

Sanes[6] rightly points out that the same patient will give a different history on different occasions. I have frequently noted a wide divergence in the statements made by the same patient to a member of the out-patient department, to the interne in the hospital, and later to a senior consultant. A second thought should also make one skeptical of a biologic phenomenon which reputedly recurs like clockwork every so many days. Corner,[8] Allen,[9] and Hartman[10] have clearly shown the marked variation in the length of the menstrual cycles of the macacus rhesus monkey, and Long and Evans[11] demonstrated a similar irregularity in the estrual cycle of the white rat which is also found in the albino mouse.

Although this question is a fundamental one, few studies have been conducted where careful detailed records of the menses were kept.

The first was reported by Foster[12] in 1889 and was based on 56 subjects, of whom 20 had previously borne children. He pointed out that the duration of the menstrual interval generally varied from month to month, and that of 380 periods observed, only 45 had occurred after an interval of twenty-eight days, while 225 took place after a shorter time (the shortest of sixteen days) and 110 after a longer interval (the longest of forty-six days). It is of interest to note the pertinacity with which traditional superstitions are held by our profession, for apparently little attention was paid to this noteworthy contribution and the main theme of the discussions that followed its presentation was that the subjects possibly had uterine or ovarian disease. In 1926 King[13] gave an analysis of 523 menstrual cycles observed in 17 subjects, 16 of whom were college women. In this case, the cycles again were found to differ greatly in length, and varied between eighteen and fifty-three days, although the majority fell between twenty-three and thirty-six days. The most frequent interval was of twenty-seven days' duration and occurred 97 times. In 1930 Geist[14] reported a marked variation in the cycles of 200 patients whose menses had been recorded for one year. Although he did not give details of individual cases, he noted that periods occurred up to five days before or ten days later than the expected twenty-eight days. A fourth study of this nature has not as yet been published, but the results were recently shown to me by Dr. C. G. Hartman of the Carnegie Institution. It was conducted by Dr. Josephine Ball of the Phipps Psychiatric Clinic, Johns Hopkins Medical School, in a group of young girls in a State Reform School and corroborates the finding of marked variability in the length of successive menstrual cycles.

The present study was undertaken with the cooperation of the Stanford School of Nursing, and the work was supervised by Dr. Ethel D. Owen who interviewed the nurses personally. Small calendars were distributed, and each individual crossed off the days of her menstrual periods. Since it is a well-recognized fact that young women entering institutional life such as a nursing school, frequently undergo marked

menstrual irregularities and have indefinite periods of amenorrhea, an attempt was made to eliminate such cases from this series. All those with periods of amenorrhea were thus seen by Dr. Owen at the termination of the study and a careful investigation was made of their menstrual histories prior to entering the school. As a result, the records of 6 nurses with periods of amenorrhea and one with prolonged uterine hemorrhage were not considered in the series as it seemed possible that the abnormality was due to a change in the individual's mode of life.

TABLE I*

NO.	GROUP	AGE	AGE AT PUBERTY	MONTHS OBSERVED	LENGTH OF CYCLES IN DAYS
1	A-1	20	13	9	28-29-30-27-29-27-29-25-29
2	A-1	19	13	9	27-31-32-27-29-28-26-28-30
3	A-1	23	13	13	28-25-26-30-27-26-27-26-27-28-27-26-28-31-28
10	A-2	23	13	13	22-18-19-18-21-17-21-20-19-19-19-19-22-22-26-19-23-21
11	A-2	22	13	13	26-26-25-25-26-24-24-23-27-23-25-23-23-25-24-26
17	A-3	19	12	13	29-30-33-30-30-32-30-31-22-34-33
21	A-3	25	14	13	32-31-31-31-30-30-34-36-31-28-31-29
22	A-3	20	13	13	36-37-31-32-31-29-30-31-30-30-31
29	B-1	22	13	9	22-24-25-24-21-28-14-21-20-22-21-21-17
31	B-1	20	12	10	28-25-21-25-20-24-20-23-20-24-21-23
36	B-2	20	14	13	31-43-48-104-53-29
37	B-2	20	14	13	41-32-31-38-27-26-47-33-39-29-27-30
45	B-2	21	13	13	54-55-42-41-32-52-38-43
52	B-3	20	13	13	19-20-22-26-20-26-26-27-28-27-26-26-54
55	B-3	20	12	10	30-25-24-14-11-21-20-22-23-22-28-20-31
60	B-3	20	12	13	28-32-29-34-34-24-36-34-29-35-33-27
64	B-3	20	12	10	38-31-30-33-56-33-28-17-33
66	B-3	18	13	13	17-12-14-13-18-23-35-27-27-26 25-23-31-68-11-15

*Examples of various types of menstrual histories. In Group A-1, the cycles were considered as regular and were of from twenty-six to thirty days in length; A-2, regular, tend to be shorter than twenty-six to thirty days; A-3, regular, tend to be longer than twenty-six to thirty days; B-1, irregular, all cycles shorter than thirty days; B-2, irregular, all longer than twenty-six days; B-3, irregular, some cycles longer than twenty-six, and some shorter than thirty days.

A total of 83 complete records covering periods of observation varying from six to thirteen months are available for study, and of these, 7 were eliminated for reasons outlined in the preceding paragraph. The final statistics are thus based on 76 subjects, with a total of 747 menstrual cycles, each cycle being considered as the period from the onset of one menstrual flow to the next. The ages varied from eighteen to twenty-nine years, with a mean of twenty and one-half years. The length of time that had elapsed since the onset of the menses varied between four and thirteen years, with an average of seven and three-tenths years, so that any irregularity noted cannot be assigned to a puberty disturbance.

A statistical study of the 747 cycles at once demonstrates a tremendous variability, the range extending from eleven to over 144

days. The most frequent cycle noted (the mode) was of twenty-nine days with 73 instances, and the next was twenty-eight days with 72 instances. The mean of all the cycles was thirty and four-tenths days, and the standard deviation was found to be ± 11.53 days. This period thus extends between eighteen and forty-two days and includes 97 per cent of all the cycles. These results conform very closely to those previously reported by Foster and King.

An analysis of the characteristics of the periods in individual cases is even more striking in demonstrating the marked variation in the length of successive cycles, and in order to classify the subjects into definite groups certain arbitrary standards were adopted. In the first category, the "Regular Group," were placed the cases in whom all the cycles fell within a five-day range, but allowing two exceptions.

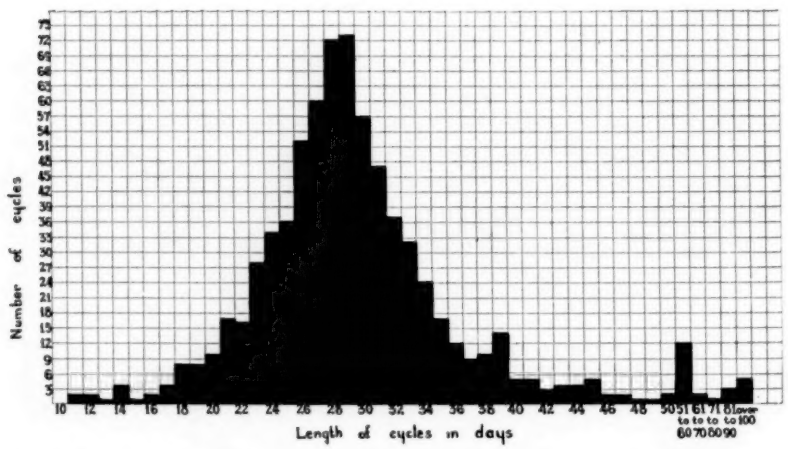


Fig. 1.—Diagram showing the distribution of the lengths of 747 menstrual cycles observed in 76 healthy young California women.

Even with this somewhat loose interpretation of what constitutes regularity only 28, or one-third, of the cases fell in this division, and it is of interest that if one or two exceptions had not been made for cycles falling outside the five-day grouping only 5 subjects with successive regular cycles would have been reported. This first main group was also subdivided into (1) the length of the cycles varied between twenty-six and thirty days (9 cases); (2) the range tended to be shorter than twenty-six to thirty days (6 cases); and (3) the cycles were generally longer than twenty-six to thirty days (13 cases).

The second main division of the classification was the "Irregular Group," and included those cases where 3 or more cycles did not fall in a five-day range with the balance of the observations. Forty-eight, or two-thirds, of the subjects were placed in this category, which was again subdivided into (1) irregular cycles with all instances shorter than thirty days (4 cases); (2) irregular cycles with all instances

longer than twenty-six days (16 cases); and (3) irregular cycles, some shorter than twenty-six, and some longer than thirty days in duration (28 cases).

Since the duration of the menstrual hemorrhage is of importance in the study of pathologic conditions, the figures for 823 menstrual periods were analyzed (Table II). The vast majority of instances varied from three to seven days, and the average for the whole series was four and six-tenths days. A study of the duration of the menses in the various subgroups showed very little difference so that the length of the cycle apparently does not influence the duration of the flow, which is a fairly constant factor in most individuals. From this it would seem that any marked deviation in the length of the menstrual periods is of more significance as evidence of abnormality than an irregularity in the length of the cycle itself (Fluhmann[15]).

TABLE II. LENGTH OF MENSTRUAL PERIODS

DURATION OF FLOW IN DAYS	REGULAR CYCLES			IRREGULAR CYCLES			TOTAL
	GROUP 1	GROUP 2	GROUP 3	GROUP 1	GROUP 2	GROUP 3	
1					3		3
2		1			4	4	9
3	3	2	4	9	20	48	86
4	27	47	49	15	34	99	271
5	34	28	52	10	61	127	312
6	16		18	6	15	50	105
7	5		12	7	3	4	31
8	1		1			2	4
9						1	1
10						1	1
Average	4.9	4.3	4.9	4.7	4.4	4.6	
Average	4.7			4.5			
Average	4.6						

A careful analysis of the length of the menstrual cycles of a group of healthy young California women living under identical conditions, has thus failed to validate the traditional teaching on this question. It has been impossible to find any instance where numerous consecutive cycles were of the same length. It was not possible to group the subjects into twenty-eight-day types, thirty-day types, twenty-one-day types, etc. No basis was found for the conception that the duration of the cycles is generally some multiple of seven, such as fourteen, twenty-one, twenty-eight days. The menstrual periods occurred at all phases of the moon. It would thus seem essential to reconsider a number of current conceptions dealing with such problems as the time of ovulation, the relation of irregular menses to pelvic disease, and the endocrinologic factors of menstruation. The problem is one of fundamental importance in the study of the physiology and pathology of the female generative organs.

CONCLUSIONS

An analysis of 747 accurately recorded menstrual cycles of 76 healthy young California women has shown a marked variability in their length. The range extended from eleven to over one hundred days, although the vast majority was between eighteen and forty-two days. The mean was 30.4 days, and the standard deviation ± 11.53.

The individual cases were divided into two main groups. The first included 28, or one-third, of the subjects, in whom there was a certain degree of regularity in the lengths of successive menstrual cycles. Of these, 9 had cycles of twenty-six to thirty days' duration, while in 6 they tended to be shorter, and in 13 they tended to be longer than twenty-six to thirty days.

The second group comprised 48, or two-thirds, of the cases and was characterized by a marked irregularity in the lengths of successive cycles. In 4 instances all the cycles were shorter than thirty days, in 16 they were longer than twenty-six days, while in 28 they were very irregular, some being shorter than twenty-six and others longer than thirty days.

The average duration of the hemorrhage in 823 menstrual periods was four and six-tenths days. It varied from three to seven days in the majority of instances, and no relation between the length of the menstrual cycle and the duration of the flow could be demonstrated.

Since this paper was written, further evidence has been adduced pointing to the irregularity of the length of the normal human menstrual cycle (*King, J. L.*: Am. J. Obst. & Gynec. **25**: 583, 1933; *Allen, E.*: Am. J. Obst. & Gynec. **25**: 705, 1933; *Hajek, O.*: Zentralbl. f. Gynäk. **57**: 257, 1933).

REFERENCES

(1) *Schroeder, R.:* Der mensuelle Genitalzyklus und seine Störungen, in Veit-Stoeckel: Handbuch der Gynaekologie, Munich, J. F. Bergmann, 1. Part 2, 1928. (2) *Graves, W. P.:* Gynecology, ed. 4, Philadelphia, 1928, W. B. Saunders Company, p. 31. (3) *DeLee, J. B.:* Obstetrics, ed. 6, Philadelphia, 1933, W. B. Saunders Company, p. 18. (4) *Novak, E.:* Menstruation and Its Disorders, New York, 1931, D. Appleton & Co., p. 89. (5) *Kelly, H. A.:* Medical Gynecology, New York, 1908, D. Appleton & Co., pp. 85, 86. (6) *Sanes, K. I.:* Am. J. Obst. & Dis. Women & Child. **73**: 93, 1916. (7) *Heyn, A.:* Ztschr. f. Geburtsh. u. Gynäk. **18**: 136, 1920. (8) *Corner, G. W.*: Contrib. to Embryol. **15**: 73, 1923. (9) *Allen, E.:* Contrib. to Embryol. **19**: 1, 1927. (10) *Hartman, C. G.:* Contrib. to Embryol. p. 1, 1932. (11) *Long, J. A., and Evans, H. M.:* Mem. Univ. California **6**: 46, 1922. (12) *Foster, E. F.:* N. Y. Med. J. **49**: 610, 1889. (13) *King, J. L.:* Contrib. to Embryol. **18**: 79, 1926. (14) *Geist, S. H.:* Am. J. Obst. & Gynec. **20**: 320, 1930. (15) *Fluhmann, C. F.:* In press.

SICKLE CELL ANEMIA IN PREGNANCY

A. F. Lash, M.D., Ph.D., Chicago, Ill.

(From the Departments of Obstetrics and Pathology of the Cook County Hospital, and the Department of Obstetrics and Gynecology of the University of Illinois)

SINCE sickle cell anemia in pregnancy has been mentioned only twice in the literature, the study of an active case with a full-term pregnancy and of the postmortem findings merited publication.

Sydenstricker found that the disease was present and recognizable at birth. On two occasions blood from the cord and from the proper circulation of the infants of "sickle cell" mothers has been found to present the specific changes. Inasmuch as Anderson and Ware published a review of the literature on sickle cell anemia in November, 1932, repetition of the literature is not warranted. However, the essential characteristics may be repeated. Although Dresbach's case of 1904 is considered the first to be published, Herrick described the condition quite completely in 1910. Since then more than forty cases of active sickle cell anemia have been reported, and more than a hundred or more were mentioned. Only two cases have been reported outside of the United States.

As to the etiology of sickle cell anemia, it is a familial disease, although sporadic cases have occurred. It appears to be transmitted by the mendelian law as a dominant factor. It occurs more frequently in males and chiefly in young people and in negroes.

Jaffe, in describing the pathogenesis, has shown the change from round to sickle cells to occur in the organs of the reticuloendothelial system, especially in the spleen and to a marked extent in the bone marrow and the liver. From an analysis of the findings, it was suggested by Anderson and Ware, that a logical sequence of events was as follows: Young erythrocytes were transformed into sickle cells in the spleen, liver, bone marrow, and as fast as they were released into the blood stream, they were phagocytosed as foreign bodies. Ninety per cent of the supply of new red cells were sickle cells. When they were put into circulation, all except about 2 per cent of the sickle cells were destroyed by phagocytosis. This brought about a greater activity of the bone marrow in the production of new cells, as was indicated by the increase in reticulocytes. The spleen and liver enlarged to take care of the influx of young cells and a vicious cycle was established. As fast as the red cells formed, they became sickle cells and were phagocytosed. The bone marrow unable to continue its hyperactivity indefinitely, and as the disease progressed, fewer new cells were put into circulation. The stimulus that caused the spleen to enlarge was thus removed and it decreased in size. The liver, however, remained enlarged, possibly because its various other functions made it less responsive to the failure of the hematopoietic system. All of the common symptoms of the disease may be explained on the basis of the above theory.

The mechanism of the formation of the sickle cells has been explained by several theories each having a certain amount of experimental support.

The essential pathology was found in the spleen, the bone marrow, and the liver. The spleen was dark red and firm; the capsule was rough and thickened. The size of the spleen varied widely, from 2.4 gm. (Steinberg) to 621 gm. (Landon and Lyman). The splenic sinuses were distended with red cells and atrophy of the pulp occurred. The malpighian bodies were small and small hemorrhagic areas were present.

The liver was nearly always enlarged; the sinusoids were somewhat dilated and contained many blood cells, both normal and sickle cells. Phagocytosis of the latter by Kupffer cells were noted.

The bone marrow was hyperplastic, with a great number of sickle cells and nucleated red cells. Steinberg has described the pathology in detail.

The symptomatology was characterized by a history of repeated attacks of weakness, jaundice, fever, and abdominal or articular pain. There was usually a history of repeated acute infections of the respiratory tract which were generally longer in duration than in normal persons.

The most common physical findings were: greenish yellow sclera, heart murmur, enlargement of the liver, adenopathy, enlarged heart, ulcer of the leg, pulmonary disease, enlarged spleen and infantile genitalia.

The blood picture was the most characteristic and diagnostic feature of the disease. The average count was from 2,000,000 to 2,500,000 although it varied from less than 1,000,000 to as high as 3,500,000. The hemoglobin varied in proportion to the red cells, averaging around 40 to 50 per cent. Nucleated red cells were generally seen, and the percentage of reticulated red cells was increased to from 10 to 15 per cent or more in most cases. Sickle cells were present, in the average case as seen in the stained smears varied from 0.5 to 4 per cent of the cells actually present in the blood stream. Moist preparations of fresh blood, inoculated for from six to twenty-four hours, showed from 50 to 100 per cent sickle cells. There was a moderate leucocytosis, polymorphonuclears predominating.

The treatment for sickle cell anemia is still in the experimental stage. The acute exacerbations appear to be benefited by rest in bed and supportive treatment. Transfusions cause only temporary improvement. Splenectomy has been advocated, but it has been found that while there is temporary improvement, the patient gradually sinks into his previous condition in from four to twelve months and continues to show sickle cells. The liver diet appears to offer more hope than any other treatment known at present.

As to the prognosis of this disease, few of the patients lived beyond the age of thirty years. Because of their general weakness and lack of resistance, patients with this condition easily succumb to the various intercurrent illnesses to which they are subject.

Although abdominal pain was mentioned in most of the cases reported, it assumes more importance from the obstetric and surgical point of view, since it may be confused with an acute abdomen. Yater and Mollari report the case of a negress, twenty-five years of age, who developed severe pain in the right side of the abdomen and in the region of the liver and suddenly vomited. The abdomen was soft, not tender and slightly distended with gas. There was some resistance in the right upper quadrant, probably due to the liver. The temperature was 99° F., pulse 110, and leucocytosis 15,000. Three weeks before this attack she was in the hospital because of a miscarriage of a six months' pregnancy, pain in both legs, and a secondary anemia.

Eighteen hours after the onset of her acute attack, she died with a clear sensorium.

Autopsy revealed the usual pathologic changes of sickle cell anemia. The authors believed that the patient died during an "abdominal crisis" apparently as the result of an arterial thrombosis of the liver, but there was insufficient evidence to substantiate this point.

Leivy and Schnabel report three cases with abdominal crises and discuss the possibility of operation being done and no pathology being found. They suggest root pains as a cause for the paroxysmal crises of pain and rigidity based on marked bony changes in the vertebras in one of their cases. But they admit that no explanations, so far given, adequately explain the abdominal crises under consideration.

The case report of pregnancy and sickle cell anemia follows:

A colored primipara, twenty-one years of age, entered the Cook County Hospital on Oct. 24, 1932, with the diagnosis of pregnancy, hypertension and asthma. Her feet had been swollen at times. She had been under observation in the prenatal clinic from July 27 to Oct. 24, 1932. Her last menstruation was on Feb. 18, 1932. She had had pneumonia and some operation on her back. Her father and mother were dead. The essential findings at her first examination were: Blood pressure, systolic 116, diastolic 84; somewhat enlarged heart and generalized dry, squeaky râles which were considered evidence of bronchial asthma. Her blood pressure gradually rose to 145 over 105, although her urinalyses were negative. Because of this hypertension she was sent into the hospital.

Physical examination found a blood pressure of 140/86, temperature 98°, pulse 120 which later dropped to 92, and respirations 22. Head and chest examination revealed only wheezing râles scattered throughout the lung area. The abdomen was protuberant, the fundus uteri being two fingerbreadths below the xiphoid process. Fetal parts could not be defined because of the large amount of fluid. Heart tones were heard in the left lower quadrant. Rectal (digital) exploration found only the soft, closed cervix. The pelvic measurements were I.S. 20, IC. 25, I.T. 31, C.D. 20; x-ray plate showed one baby with the head above the pelvic inlet. Urinalysis found normal findings. Vaginal smear revealed no gonococci. Kahn test was negative.

On Oct. 29, 1932, at 10:00 A.M. labor began. Pains became severe twenty-four hours later and she vomited. Sleep was induced with morphine and scopolamine. Vomiting recurred several times. Normal saline (1800 c.c.) was given hypodermically, forty-eight hours after the onset of labor, followed by 25 per cent dextrose solution (200 c.c.) intravenously. One-half hour later the patient had a chill lasting ten minutes and her temperature rose to 104° F., pulse to 140, and respirations to 48. The blood picture, one-half hour after the chill, was hemoglobin 75 per cent, R.B.C. 3,450,000, W.B.C. 39,600. Stimulants were administered. B.O.W. ruptured spontaneously fifty-two hours after the onset of labor. It now became evident that there was a disproportion present and the head could not be impressed by the Hillis maneuver. The cervix was dilated 5 cm. Therefore a cesarean section was indicated.

Under local anesthesia (1 per cent novocaine, infiltration) a cervical cesarean section was done. It was observed that the patient responded little or not at all to stimuli. A live baby was extracted and the operation was completed uneventfully. The conjungata vera measured directly through the operative wound was 8.0 cm. The biparietal diameter of the baby's head was 10.0 cm. The patient remained in a stuporous condition and in spite of stimulation continued to run a rapid pulse until death which occurred six hours after operation. The patient's condition appeared to remain the same from the time she had the chill after the injection of the glucose. The baby weighed 7 pounds, 1½ ounces. Sickle cells were found in the blood smears of the baby (moist preparation after twenty-four hours).

Essential findings at autopsy (by Dr. Victor Levine of the Pathology Department) were as follows: the liver was 9 cm. below the xiphoid and 5 cm. below the right costal margin. The spleen was much enlarged and the lower pole was 9 cm. below the left costal margin. The uterus extended 14 cm. above the symphysis pubis. In the visceral pelvic peritoneum over the lower uterine segment there was a recently sutured transverse 6 cm. incision.

In the right pleural cavity there were focal fibrous adhesions over the anterior surface of the lung and diffuse fibrous adhesions over the posterior surface, apex and base.

The lungs were pink gray and crepitant throughout. The cut surfaces were light gray mottled with red gray. Frothy fluid was expressible.

The heart was light purple gray, weighing 280 gm. The myocardium was fairly firm.

The spleen weighed 960 gm., was very firm, dark purple gray and measured 26 by 11 by 7 cm. in the various diameters. The lymph nodes at the hilus were enlarged up to 2 cm., were soft, purple mottled with yellow. The external surface of the spleen contained numerous small depressions, largest 2 mm. in diameter and 1 mm. deep. The cut surface showed the pulp to be firm and deep purple; the trabeculae were distinct.

The liver weighed 2420 gm., was deep purple and quite firm. The cut surface was a light brownish purple. The markings were absent.

The kidneys weighed 330 gm., were soft and the capsule stripped readily leaving a smooth purple gray surface. The cut surface showed the cortex to be purple gray, 5 mm. thick; the markings were absent; the glomeruli were prominent and many of them appeared as bright purple pinpoint specks. The medulla had the same color. The pelvic mucosa was light gray with a few 1 mm. red areas.

The uterus showed the usual characteristics of an emptied, full-term uterus with a recently sutured lower uterine cesarean section wound.

The bone marrow was a deep purple and soft.

The microscopic examination of the essential structures revealed the following: The bone marrow was very cellular and the fat tissue was much reduced by numerous focal areas which were composed of neutrophilic myelocytes and metamyelocytes, oxyphilic myelocytes and leucocytes, and of erythroblasts and normoblasts. The erythropoietic and granulopoietic tissue were about even in amount. The nucleated red cells were round and showed no signs of disfiguration. Scattered between the nucleated red cells, there were a few hematogonia, with deeply basophilic cytoplasm. Megakaryocytes were fairly numerous, and some of them showed a pyknosis of the nucleus. The reticular cells contained a few engulfed red blood cells and a moderate amount of pigment.

The splenic pulp was enormously engorged by red blood, practically all of which showed a distinct sickle shape. The sickle cells filled the sinuses as well as the reticulum of the cords. The other cells were very scanty. There were a moderate number of nucleated red cells and of lymphocytes, and single free histocytes containing red blood corpuscles. The follicles were small and lymphocytic.

In the liver, the portal capillaries were stuffed by sickle cells which formed dense clumps and were often enclosed in huge Kupffer cells. There were also round normoblasts, polymorphonuclear leucocytes and free histocytes in the portal capillaries besides the sickle cells. The liver cells were fairly well preserved and contained a moderate amount of brownish pigment granules.

The glomerular tufts of the kidneys were very prominent because they were stuffed by sickle shaped erythrocytes. The tubular epithelium was swollen and in a few places small brownish pigment granules could be seen near the basement membrane.

In the lungs the alveolar capillaries were wide and filled by sickle shaped blood cells. The alveoli and alveolar ducts were very wide and some of them contained an homogeneous pale-stained material mixed with mononuclear cells.

The large size of the spleen indicated the marked acute activity of the pathologic process.

In view of Moon and Kennedy's findings in shock, which were characteristic widespread vascular phenomena (dilatation and engorgement of capillaries and vessels, and permeability of capillary walls) most prominently seen in the pulmonary and gastrointestinal tracts, the cause of death of the patient (E. H.) was shock, because the postmortem examination revealed these findings, especially in the lungs. These circulatory effects may be produced by various factors (Moon-Kennedy-trauma, intravenous or intraperitoneal injections of extract of normal muscle, etc.). In this specific instance, a prolonged labor, the reaction from the intravenous injection of the hypertonic glucose solution, a cesarean operation, and an active sickle cell anemia were sufficent causes for shock.

DISCUSSION

Although the characteristic pathologic findings were present in the patient the diagnosis was only made at autopsy. The importance of recognizing such a condition clinically is evident. Because a labor may be long and exhausting, the delivery may be operative and require a good defense mechanism to overcome the potential infection. However, secondary anemia, pains in the legs and occasional weakness are not uncommon symptoms during an apparently normal pregnancy, although these symptoms may be the only subjective evidence of sickle cell anemia. The diagnosis of sickle cell anemia would depend entirely on finding the sickle cells in the circulating blood or in moist preparations of fresh blood standing for about twenty-four hours. Since the liver diet offers at present, more hope than any other treatment for sickle cell anemia, and since it appears so difficult to diagnose during pregnancy, it seems logical to suggest that in all secondary anemias of pregnancy, the liver diet should be instituted. Thus the simple secondary anemias may be overcome as well as the undiagnosed sickle cell anemia.

This procedure is essential to build up the patient's resistance, because operation may be imperative as in this patient in whom there was a definite disproportion between the occiput and the inlet of the pelvis.

The cause of death in this patient is not certain, although shock is given as the cause. Because the condition of the patient before the operation was the same as after, the operation was done under local anesthesia and did not appear to be disturbing, even when judged from experiences with other patients and the same operation. It,

therefore, seems, from impression only, that the factor which caused this patient's death was acting even before the operation. This death-producing factor is unknown and is probably present in these patients dying during an "abdominal crisis" in the course of a sickle cell anemia. It is also probable that a preeclampsia of pregnancy may have been an added factor.

SUMMARY

1. A full-term pregnancy occurred in the course of an active or activated sickle cell anemia. Death followed a long labor and a cesarean section in six hours.

2. The baby survived and showed sickle cells in moist preparations of fresh blood (after twenty-four hours).

3. The autopsy findings were characteristic of sickle cell anemia. The spleen weighed 960 gm., the largest spleen reported in the literature.

4. The diagnosis of this condition clinically and the cause of death are discussed.

30 N. MICHIGAN AVENUE

REFERENCES

Anderson, W. W., and Ware, R. L.: Am. J. Dis. Child. **44:** 1055, 1932. *Dresbach:* Science **19:** 469, 1904 and ibid. **21:** 473, 1904. *Herrick, J.:* Arch. Int. Med. **6:** 517, 1910. *Jaffe, R. H.:* Virchows Arch. f. path. Anat. **265:** 452, 1927. *Landon and Lyman:* Am. J. M. Sc. **178:** 223, 1929. *Leivy, F. E., and Schnabel, T. G.:* Am. J. M. Sc. **83:** 381, 1932. *Moon, V. H., and Kennedy, P. G.:* Arch. Path. **14:** 360, 1932. *Steinberg, B.:* Arch. Path. **9:** 876, 1930. *Sydenstricker, V. P.:* J. A. M. A. **83:** 12, 1924. *Yater, W. M., and Mollari, M.:* J. A. M. A. **96:** 1671, 1931.

PLACENTAL NECROSIS

ALFRED B. CLEMENTS, B.S., M.D., NEW YORK, N. Y.

(From the Department of Pathology, Bronx Hospital)

THE study of placental infarction or, to use what we consider to be the more correct term, placental necrosis, has been the subject of considerable research by clinicians, pathologists and roentgenologists, with results which are quite inconclusive. I wish herewith to present and to correlate certain clinical and pathologic findings associated with the occurrence of placental necrosis in 500 cases which have been studied in this laboratory.

It is generally conceded that an infarct is an area of coagulation necrosis resulting from the arrest of circulation in the artery supplying the part. Thus, obstruction of an end artery in an organ, such as the liver, kidney, or spleen, results in starvation of that part whose nutrition was supplied by the occluded vessel, causing death of tissue

with a more or less characteristic infarct formation. It is the opinion of many observers that the pathologic process involved in placental infarction, however, is of an entirely different nature.

The circulation in the human placenta entails two separate and distinct systems, fetal and maternal, with no direct communication between them. The interchange of metabolic products occurs through the biochemical processes of osmosis and diffusion. It has been quite conclusively established that the chorionic villi depend on maternal blood for their nourishment and growth. Pathologic change in villous vessels therefore does not account for placental necrosis. In proof of this, the following facts have been advanced by Young:

First: Chorionic elements are most active during the early stages of development before fetal vessels are formed.

Second: Hyperplastic chorionic epithelium is present to its greatest extent in hydatid mole and chorionepithelioma where few fetal vessels are present.

Third: Tips of villi remain healthy in tubal pregnancy where the blood supply from the ovum has been cut off by hemorrhage but where the maternal circulation is unimpaired.

Fourth: Fragments of undegenerated syncytium have been transplanted by the maternal blood stream to various organs of the pregnant woman and have retained their vitality.

Fifth: Marked endarteritis of villous capillaries, as seen in syphilis, is not associated with increase in incidence of necrosis.

In view of the above, it is apparent that necrosis of the placenta cannot be explained by changes in the vessels supplying the villi. We are led therefore to believe that the necrosis is due to a deficiency of maternal blood. We must next determine whether this interference is a local manifestation of a systemic condition or originates in situ. Embolism of bacteria and their products from foci of infection elsewhere in the body especially from infected tonsils, teeth, and sinuses has been proposed by many as a systemic cause. Talbot advances the theory that hematogenous infection causes thrombosis of uterine blood sinuses, thus depriving that portion of nutrition and causing necrosis. In refutation, it may be stated that no relation between actual lesions of acute inflammation and occurrence of necrosis has been observed. This fact was substantiated in our investigation, as will be shown later. Histologic studies of necrotic areas rarely show infiltration by polymorphonuclear leucocytes as found in areas affected by bacterial embolism.

Changes in the vessels of the decidua with resulting vascular occlusion has been advanced as another explanation. Recent research has shown that the decidual arteries discharge their blood into a subchorial space which communicates freely between the villous stems. The blood is then recollected by the decidual veins. The villi are thus bathed in a pool of maternal blood rather than by any individual blood vessel, so that it appears unlikely that interference with the circula-

tion in one or more decidual arteries can affect placental nourishment. A possible exception to this, as has been pointed out by many observers, is marginal necrosis due to deficiency in blood supply at the edge of the placenta. This is further substantiated by recent roentgenologic studies of Thoms showing that, especially in the latter months of pregnancy, the maternal circulation appears insufficient to nourish the chorionic villi at the margin of the placenta.

The most plausible theory and the one that most readily lends itself to correlation with the clinical findings is that the process is a local phenomenon in the form of degeneration of the syncytium resulting in coagulation of the intervillous blood. It is believed that one or more constituents of the maternal blood are responsible for the degeneration of the villous epithelium. Some attribute this to an endothelial poison circulating in the maternal blood which, when in sufficient concentration, destroys the syncytium, clotting the blood over and around the villi. A modification of this theory is that a hormone-like substance has, as its function, the checking of the invasive nature of the chorionic epithelium, which function is performed during the early months of pregnancy by the Langhans layer. During the latter months, this layer gradually disappears and coincidentally, necrotic areas appear more frequently. Thus the process of necrosis is apparently a physiologic one. The probability exists that insufficient hormone, on the one hand, may lead to chorionepithelioma while excessive hormone, on the other hand, causes widespread necrosis.

With the formation of a thrombus, the area of placenta lying in immediate contact with it is deprived of maternal blood supply and necrosis occurs. The process begins with small areas of tissue death rather than with infarction, in the commonly accepted sense of the term. Grossly, the picture is that of a "red infarct." Microscopically, these areas contain dilated, engorged capillaries. Some of these can be seen to have ruptured, pouring out red blood cells and fibrin ferment. Coagulation necrosis of numerous affected villi occurs which progresses so that only traces of the previously existing villi remain. The red cells and fibrin deposits disintegrate and are subsequently absorbed. Hyalinization occurs, changing the gross color from red to white. In advanced stages there is seen varying degrees of calcification.

Thus the color of the "red infarct" is not due to hemorrhage but to dilatation and engorgement of villous capillaries with fetal blood. The subsequent pathologic processes are similar to those observed elsewhere when thrombosis and necrosis have taken place. These stages have been thoroughly decribed by Hitschmann and Lindenthal, Montgomery and others and need not be discussed here at length.

Numerous investigators have propounded a causal relationship between maternal toxemia and placental necrosis. This belief has reached

a widespread acceptance. The frequency of such an etiology for necrosis will be considered later. In cases associated with chronic nephritis, one encounters actual instances of placental apoplexy with formation of hematomas as seen in other organs. These placental hematomas are rarely fetal in origin; they occur as the result of the rupture of maternal vessels, the mechanism being similar to that of uteroplacental apoplexy.

With the above theoretical considerations in mind, a gross analysis was made of 500 consecutively delivered placentas from the Obstetrical Department of the Bronx Hospital, supplemented by microscopic examination. Of these, 442 were from service patients and 58 from patients delivered by private physicians. Among the former, only those were included who had had careful prenatal attention. These patients during their puerperium were interviewed personally to prevent any omissions that may possibly have occurred in recording their antenatal history. The records of the private patients were obtained from their family physicians and added to the group only when considered to be complete.

The following points were noted:

1. Rise in systolic blood pressure (130 mm. being considered high normal).
2. Albuminuria (other than an occasional faint trace).
3. Headaches and dizziness.
4. Spots before the eyes.
5. Edema of the hands, feet, and face.
6. Upper respiratory and dental infections.
7. Maturity of gestation.

The first five symptoms and signs were considered indicative of a toxemic condition. Graphically, the results obtained are summarized by Table I. It will be seen that the percentage frequency of necrosis in the total series, in those patients with a history of toxemia and in those who had had upper respiratory infections is remarkably similar. A few exceptional cases noted in this series follow; only relevant symptoms are mentioned:

TABLE I. SUMMARY OF GROSS FINDINGS

Total number of cases	500
Percentage of cases showing gross evidence of infarction (1 cm. or more in diameter)	68.6
Number of cases showing symptoms of toxemia	123
Percentage of patients with toxemic symptoms showing gross evidence of infarction	65.8 (81)
Number of cases with upper respiratory infection	40
Percentage of patients with upper respiratory infection showing gross evidence of infarction	67.5 (27)

CASE 1.—Mrs. M. P., para i, history negative. Placenta showed two "white infarcts" eccentrically situated, 5 by 4 and 6 by 4 cm. in diameter and two 1 cm. marginal "infarcts."

CASE 2.—Mrs. E. R., para i, history negative. Placenta showed one "red infarct," marginal in location, measuring 3 by 2 cm. in its largest diameters and two marginal "white infarcts" 1 cm. in diameter.

CASE 3.—Mrs. C. F., para ii, gravida iii. Patient had an acute upper respiratory infection with fever, lasting about three weeks, during the eighth month of pregnancy. Placenta showed no gross abnormality.

CASE 4.—Mrs. F. S., para i. Patient had lobar pneumonia during the fourth month of pregnancy lasting six weeks. Complicated by pleurisy with slight effusion. Placenta showed no gross abnormality.

CASE 5.—Mrs. H. L., para i, gravida iv. Blood pressure rose to 160/100 in prenatal clinic, was 195/120 on day preceding delivery. Patient complained of heartburn, severe headaches and had a moderate degree of ankle edema. Examination of fundi negative. Placenta showed a single submiliary marginal "infarct."

CASE 6.—Mrs. C. W., para ii. Suffered with severe headaches, dizziness, spots before the eyes, and heartburn during the entire pregnancy. Blood pressure only moderately elevated but patient had a convulsion on the delivery table lasting three minutes. Placenta showed a pinhead size marginal "white infarct."

It was noted during the gross examination of the placentas and in their microscopic study that the areas of necrosis showed increased amounts of calcium deposition. In addition, a certain percentage of the placentas showed varying amounts of what we termed "spider web formation." These fibrillar deposits on the maternal surface, which assumed a spider web appearance, grossly and chemically contained a large amount of calcium. Calcium determinations were then made upon areas of necrosis, areas of spider web formation and areas of normal mature placental tissue (Table II).

TABLE II. CALCIUM DETERMINATIONS

CASE	SOURCE	WT. OF DRIED SAMPLE (GM.)	WT. OF CA. IN SAMPLE (GM.)	PER CENT CA.	BLOOD CA. MG./100 C.C.
460	Anemic necrosis	0.3059	0.0122	3.98	9.2
463	Anemic necrosis	0.1389	0.00641	4.61	Not estimated.
495	Spider web formation	0.4358	0.0794	18.22	8.9
271	Anemic necrosis	0.3160	0.00357	1.13	Not estimated.
268	Anemic necrosis	0.147	0.0106	7.21	Not estimated.
468	Normal mature placenta	1.0934	0.00541	0.494	9.4
499	Normal mature placenta	2.0738	0.00225	0.108	9.2

These calcium figures appear to support the idea of Fraser that the placenta in the latter months of pregnancy undergoes what he terms a "physiologic vascular senescence," i.e., at term the placenta is definitely a senile organ, reaching the limit of its usefulness and presenting signs seen in other senescent organs, including increasing amounts of calcium deposition. The spider web formation was observed almost invariably in full-term or postmature placentas.

CONCLUSIONS

1. Areas of necrosis measuring 1 cm. or more in diameter were observed in 68.6 per cent of all placentas examined. It is believed that the amount of circulatory disturbances at the edge of the placenta as the result of such necrosis is so slight as to be negligible.

2. More than 50 per cent showed small white necrotic areas on the fetal surface. These are for the most part surface affairs and of no clinical significance.

3. There was no apparent increased tendency to necrosis in the toxemias of pregnancy. Markedly toxic patients and preeclamptics were observed without apparent placental change while there were many placentas with advanced necrotic changes and a completely negative history.

4. There was no apparent relationship between placental necrosis and systemic infections including those of the upper respiratory system.

5. The histopathologic picture of these infarcts is described.

The author is indebted to Dr. Joseph Felsen, Director of Laboratories, Bronx Hospital, for his encouragement and suggestions in the carrying out of these studies.

REFERENCES

(1) *Cantarow, A., Montgomery, T. L., and Bolton, W. W.:* Surg. Gynec. Obst. **51:** 469, 1930. (2) *Clemenz, E.:* Ztschr. f. Geburtsh. u. Gynäk. **84:** 768, 1922. (3) *Fraser, John:* Am. J. Obst. & Gynec. 6: 645, 1923. (4) *Montgomery, T. L.:* Am. J. Obst. & Gynec. **21:** 157, 1931. (5) *Talbot, John E.:* Surg. Gynec. Obst. **32:** 552, 1921. (6) *Thoms, Herbert:* Am. J. Obst. & Gynec. **17:** 176, 1929. (7) *Young, James:* J. Obst. Gynec. Brit. Emp. **26:** 1, 1914.

1505 Boston Road

A MODIFICATION IN TECHNIC OF THE BELL-BEUTTNER OPERATION*

Frederick H. Falls, M.D., Chicago, Ill.

(From the Department of Obstetrics and Gynecology, University of Illinois, College of Medicine)

ONE of the major problems in gynecology for those of us who are entrusted with the care of a large number of serious pelvic infections which have resulted in extensive pelvic peritonitis and damage to the tubes and ovaries, occasioned by lack of proper treatment, is the rehabilitation of these patients for active participation in our industrial system with the preservation of as much normal function as possible with the material at hand.

Two errors in judgment may be committed:

*Read at a meeting of the Chicago Gynecological Society, May 19, 1933.

1. Ultraconservatism leading to prolonged morbidity and too often to eventual operation when the infection has destroyed any chance that there may have been for surgical conservatism if earlier operation had been elected.

2. Ultraradicalism in which functionally capable organs are sacrificed because of minor damage, in the belief that the pathologic changes present cannot be expected to heal satisfactorily, and that conservation of tissue will result in further morbidity and ultimately in reoperation.

In 1908, Beuttner described an operation for the removal of diseased tubes in which the interstitial portion of the tubes with a wedge portion of the fundus of the uterus was removed and the wound in the uterus closed and peritonized by sewing the peritoneum from the uterovesical fold over the line of suture in the uterus. He gave as indications and conditions for this operation:

1. Bilateral salpingitis occurring in young women.

2. Cases in which conservation of at least part of one ovary was possible.

3. Metritis of the uterine corpus.

4. Such marked adnexal changes that the tubes should be removed from the midline outward according to the Faure technic. The technic of his operation is as follows:

1. A double ligature is passed through the broad ligament at the edge of the uterus from behind forward as low down as conveniently possible. The suture is cut at the needle and one end is brought back through the broad ligament and tied, which shuts off the ascending branch of the uterine artery on that side. The other half of the double ligature is used for tying off the pedicle of the round and broad ligament after removal of the tubes.

2. A transverse wedge-shaped excision of the uterine fundus with hemisection of the wedge.

3. Extirpation of the tubes from the midline outward according to Faure.

4. Closing the uterine wound by interrupted sutures and peritonizing by sewing the uterovesical fold of the peritoneum to the posterior wall of the uterus.

In 1914, Bell described a similar operation. In a discussion of the technic of the operation he describes tying off of the uterine arteries on each side about one-half to one-fourth of an inch above the level of the internal os. The arteries are exposed by raising a flap of the peritoneum of the uterovesical pouch by means of a transverse incision. This shuts off the blood supply to the upper part of the uterus and renders the operation almost bloodless. Following the excision of a transverse wedge-shaped portion of the fundus including the interstitial portion of the tubes and the uterine insertion of the round ligaments, the V-shaped raw area left in the uterus is closed by means of mattress-and-over sutures. The pedicles on each side which contain the round and upper part of the broad ligaments are sutured high on the back of the retained portion of the uterus. The flap of peritoneum which is raised from the uterovesical pouch is brought up over the line of suture on the summit of the small uterus and is sutured to the posterior wall. He stresses the peritonization because of the obvious difficulty in preventing adhesions between the top of the uterus and the intestines if the scar and mattress sutures are not covered.

In Bell's hands this has been successful as far as the conservation of the menstrual function is concerned in 90 per cent of 127 cases. In 88 of these cases the tubes were removed together with the ovaries and an ovarian graft was performed. In 19 cases the ovary was retained and of these cases 8 out of 9, in which follow-up was possible, showed a successful result. In 118 of his cases the ovaries as well as the tubes were removed because of marked degenerative changes. Portions of the ovary were grafted into the rectus sheath. Menstruation was maintained, beginning a few months after operation, from one to several years. In those cases in which it ceased there was relatively little discomfort from menopause symptoms. The principle of the operation involving the complete removal of the interstitial portions of the tubes, and that portion of the myometrium most likely to be secondarily involved, together with good peritonization and preservation of the menstrual function and the internal secretion of the ovary has always appealed to me.

There are two main objectives to the operation as described by Bell and Beuttner.

1. It is not necessary to tie off the uterine arteries near the lower uterine segment in order to give satisfactory hemostasis.

2. The uterus after the Bell-Beuttner operation frequently is found to be retroposed and somewhat lower in the pelvis than normal. This is due to the stretching of the round ligaments secondary to the retroversion of the uterus which so frequently is seen with prolapsed inflamed adnexa. It is obvious that Bell has recognized this fact and sought its correction by his method of sewing the detached round and broad ligaments to the upper part of the posterior aspect of the uterus after peritonizing the transverse line of suture. This leaves some raw areas and catgut knots exposed.

My own experience with this operation dates back to my gynecologic service at the University of Iowa in 1922. In the early cases I used the technic described by Beuttner, except that I did not tie the uterine arteries, a step that I considered both unnecessary and inadvisable. On examining these patients postoperatively, I found that there were a considerable number in whom the uterus sagged back into the hollow of the sacrum. Some of these women complained of bladder irritability and of a dragging, bearing-down sensation. Urologic consultation in a number of these cases, with and without symptoms, revealed considerable bladder distortion and in some cases decreased tolerance. It occurred to me that if the uterus could be elevated, there would be less bladder distortion, less tendency toward residual urine, and, also, less tendency to uterine prolapse with its attendant symptoms. I therefore determined to shorten the round ligaments in addition to performing the defundation. I first tried sewing the round ligaments to the anterior surface of the uterus as is done in the Coffey suspension. This necessitated pulling the peritoneal reflection and bladder over the round ligaments, which did not leave as smooth a closure as in the original operation. I next tried sewing the round ligaments to the posterior surface of the uterus after drawing the peritoneal reflection and bladder over the fundus as

in the original Beuttner technic. This also was unsatisfactory, since it left some catgut and rough peritoneum on the posterior surface of the uterus, which might give rise to adhesions. I then hit upon the plan which has given excellent service in my hands, the details of which I wish to present in this communication. The technic of the modified operation is as follows:

1. The uterus is exposed and the fundus grasped with a tenaculum.

2. The tubes and ovaries are freed from adhesions and the advisability of leaving one or both ovaries is carefully considered. I use sharp dissection with a scissors to free the adnexa in most cases and find it rarely necessary to resort to the Faure technic to free the tubes.

3. The mesosalpinx is clamped and cut above the clamp releasing the tube. The stump is ligated and the clamp removed from the top of the broad ligament.

4. Small Kocher forceps are now placed on the edge of the uterus just below the insertion of the tube to limit the bleeding until replaced by sutures.

5. A wedge-shaped incision is made in the uterine fundus down to the mucosa from side to side including the interstitial portion of the tubes. This does not include the attachment of the round ligaments to the uterus. The wedge is one to two centimeters wide at the top, depending on the size of the uterus.

6. The round ligaments are now pulled into the wedge-shaped wound left in the fundus of the uterus. This is accomplished by inserting the needle with No. 2 chromic catgut through the posterior lip of the uterine wound near its center. The point of the needle emerges close to the mucosa of the uterus and about 2 cm. below the cut edge. The needle is then passed through the broad ligaments just below the round ligament at about the junction of its middle and inner third. It is then brought back and inserted through the anterior lip of the uterine wound at about the same level as the stitch through the posterior lip. On pulling this stitch taut, the round ligament is doubled on itself and drawn into the groove of the fundus of the uterus, which closes over on top of the ligament. When the opposite round ligament is brought in the same way and the sutures tied, the uterus is found to be suspended by the shortened round ligaments which are buried in the muscle of the fundus. Two additional interrupted sutures are placed through the fundus from the posterior to the anterior wall, which also help to fix the round ligaments in place. One of these is placed near the uterine cornu, replacing the above-mentioned hemostatic forceps, the other midway between this and the first stitch. Corresponding interrupted stitches are placed on the opposite side.

Formerly, I used a continuous suture for retaining the round ligaments in the groove in the fundus, but have felt that there was less danger of bleeding with the interrupted sutures. The mattress sutures used by Bell seem quite unnecessary.

The loose peritoneal reflection of the uterovesical pouch is seized by a tissue forceps and drawn up over the wound and sewed to the posterior wall of the uterus by a continuous No. 0 catgut suture in such a way that the wound and the suture line in the uterus are completely and smoothly peritonized, leaving only one knot of fine catgut exposed, as in the original Beuttner technic. Postoperatively, these uteri are found to be held well up in the pelvis, to be freely movable, and I believe there has been less complaint of bladder disturbance and backaches since the adoption of this modification.

I have been doing this operation now for about ten years. We have examined many of these patients several years after operation and the results have been uniformly satisfactory. In these cases I have not used

the ligature around the upper part of the uterine artery which is advised by both Bell and Beuttner in their operation. My reason for this deviation is that I feel by my modified technic the anastomosing branch of the uterine artery which helps to supply the ovarian circulation is conserved, improving thereby the chance of functional survival of the ovary without jeopardizing the patient's safety by increasing the danger of hemorrhage. If there are many small bleeding vessels in the uterine wall immediately after removal of the wedge, I sometimes close the wedge-shaped cavity temporarily by approximating the edges by means of a bullet forceps. Such bleeding has never been dangerous, and is very easily controlled.

Since my return to Chicago, I have been doing the modified operation exclusively, 208 cases at the Cook County Hospital and 34 at the Research Hospital. There was one death from general peritonitis in one of the cases at the Cook County Hospital, and one death from the same cause at the Research Hospital. The bowel was injured during the freeing of the adhesions in both cases.

As a result of my experience with this operation, I have used it exclusively in cases needing double salpingectomy. The apparent advantages of this operation are:

1. That it results in smoother peritonization.
2. That it removes all of the infected tubes.
3. That it removes metritis and reduces the size of boggy uteri.
4. That it leaves the uterus, bladder, and ovaries in good position.

The advantages over the Bell-Beuttner operation are:

1. It is simpler and takes less time.
2. It preserves the anastomosing branch of the uterine arteries supplying the ovary.
3. The uterus, bladder, and ovaries are held up in better position.
4. Peritonization is simpler and smoother than in the Bell operation.

The advantages over supracervical hysterectomy are:

1. Preservation of menstruation for its psychic value in young women.
2. Longer life of retained ovaries. Graves estimates that they remain functionally active for about two years after hysterectomy.
3. The position of bladder and pelvic organs is more nearly normal than after hysterectomy.

1819 West Polk Street.

DISCUSSION

DR. CAREY CULBERTSON.—I have used this procedure for exactly twenty years, where I desired to preserve menstruation after salpingectomy. I believe the modifications of Dr. Falls would have an advantage. From the beginning I ligated and cut away the round ligaments and did not ligate the uterine artery,

and then used the round ligament to peritonize the wound in the uterine fundus. This technic has been so successful that I have continued it without any essential modifications. In 1921, I tabulated 518 cases of pelvic peritonitis which I had operated upon; 219 were done by that method. In 1931 and 1932, I performed this fundal amputation—I prefer to call it that rather than "defundation"—59 times. The operation is determined more particularly by the character of the uterus and the age of the patient. Fundal amputation is practically always done on relatively young women. In those 59 cases the youngest was seventeen—there was only one—and the oldest was thirty-five, again only one. This compares favorably with the collateral series of 48 cases in which the operation for salpingitis was accompanied by 48 hysterectomies, the ablation of the uterus depending again on the character of the organ and the age of the patient. It is not desired particularly to preserve menstruation in women over 35, especially if the uterus is diseased. Thirty-one of the 48 cases had fibroids, and only one of the 59 had a small fibroid in the fundus, and another one was not done for salpingitis but for tubal pregnancy. In addition to that, there were 5 other cases treated surgically. This does not take into consideration those cases that were treated conservatively rather than by any other method.

DR. WILLIAM C. DANFORTH.—I think the essayist failed to bring out one condition in which this operation might be used, namely, in older women who have retrodisplacement and who desire sterilization done. This can be done and part of the uterus preserved.

DR. JOSEPH L. BAER.—Mention should be made of the risk of implantation of the round ligaments into the corpus uteri and in contact with the endometrium. This step could conceivably increase operative morbidity.

DR. FALLS (closing).—Shortening the round ligaments following defundation according to the Coffey technic, interfered with smooth peritonization as did likewise the Baldy-Webster operation. Finally, I put the round ligaments down into the cavity formed by the removal of the wedge. I have been very well satisfied with the results.

I have used the procedure in cases such as Dr. Danforth mentioned in older women for sterilization. It certainly leaves a smoother peritoneal surface than if one removes the tube and drops the uterus back after whipping over the top of the broad ligament.

Answering Dr. Baer,—in the early operations I was in some doubt as to whether opening the uterine cavity would expose the peritoneal cavity to infection, but I have had no serious infection result. Two women died of peritonitis; 2 out of 254 laparotomies is not a very high percentage. I have seen only two uteri removed following this operation. There has been no evidence of infection in these cases.

BLOOD CHEMISTRY STUDIES OF NORMAL NEWBORN INFANTS*

II. Blood Sugar and Alkali Reserve Estimations

Albert Holman, M.D., and Albert Mathieu, M.D., Portland, Ore.

IN OUR previous communication,[1] we reported comparative sugar estimations on the bloods of 50 mothers and their babies at the time of birth. In the present paper we wish to give the result of a series of comparative alkali reserve and sugar estimations on the bloods of 50 mothers and their infants at delivery. (These were private patients.)

TECHNIC

As was stated in the first paper of this series, blood was taken from the maternal end of the severed cord as soon as possible after birth, and blood was simultaneously drawn from the median basilic vein of the mother. The Haskins, Holbrook[2] modification of the Schaffer microcopper method was used in all blood sugar estimations and no sample was allowed to stand over two hours before the sodium tungstate sulphuric acid filtrate was made. The Haskins, Osgood[3] modification of the Van Slyke titration method was used in determining the alkali reserve figures.†

It will be seen that the alkali reserve figures of the babies fall into normal limits, and average very little below the maternal figure, being 49.72 and 51.13 respectively. From this fact one could reason that as true acidosis is a factor in eclampsia,[4] the babies of eclamptic mothers may be born with a low alkali reserve.

The average blood sugar figure for both series with a total of 100 mothers was 100.5 mg. The average of 100 babies (first and second series) was 95.4 mg. The results of these two series of estimations establish an average for blood sugar and alkali reserve of normal mothers and their babies at delivery.‡

Our figures appear to prove quite definitely that, in normal cases, the blood sugars of the mother and her baby are practically the same. Our conjecture that this ratio is probably maintained in abnormal cases is substantiated by the following case seen in consultation. The mother, toxic in the last month of pregnancy, had received 300 c.c. of 25 per cent glucose solution fifteen minutes before delivery. Her

*Read before the Portland Society of Obstetricians and Gynecologists, January 25, 1933.

Submitted for publication, January 25, 1933.

†The alkali reserve figure is the number of cubic centimeters of dry carbon dioxide (measured at 0° C. and 760 mm. Hg) which can be held in chemical combination, excluding dissolved carbon dioxide, by 100 c.c. of plasma after exposure to an atmosphere containing 5.5 per cent carbon dioxide (alveolar air) at 20° C.

‡Blood sugar estimations are given as milligrams in 100 c.c. of blood.

blood sugar reading was 424 mg., and that of her offspring 439 mg. These figures gave evidence that glucose injected intravenously into the mother passes into the fetal circulation very rapidly.

	BLOOD SUGAR		ALKALI RESERVE	
	MOTHER	BABY	MOTHER	BABY
1	140	126	35.84	35.84
2	132	140	58.24	62.76
3	124	127	44.80	59.36
4	99	96	53.76	40.32
5	79	68	53.76	47.04
6	66	66	44.80	43.46
7	93	90	42.46	44.80
8	93	95	56.00	62.72
9	87	82	31.80	47.71
10	76	74	51.52	38.08
11	55	63	33.60	24.64
12	109	92	52.40	47.00
13	74	82	62.72	51.50
14	76	79	58.24	53.76
15	71	66	49.28	38.08
16	99	97	67.20	64.26
17	76	79	58.24	53.76
18	78	80	49.28	38.08
19	78	82	58.24	62.72
20	122	96	67.20	64.26
21	89	96	49.28	51.06
22	109	97	44.80	43.46
23	120	100	53.76	47.04
24	120	124	56.00	62.70
25	124	109	53.70	47.04
26	109	127	58.24	60.00
27	130	140	56.00	58.20
28	87	93	49.28	51.06
29	97	97	30.69	40.32
30	119	109	33.14	47.94
31	126	96	54.33	54.88
32	74	82	64.90	58.24
33	93	90	44.80	43.46
34	96	100	49.28	51.52
35	68	73	51.52	56.00
36	87	85	42.56	47.70
37	143	143	58.24	53.76
38	132	116	62.72	44.80
39	130	129	58.24	56.00
40	140	108	60.48	51.52
41	98	96	53.76	40.32
42	124	127	44.80	59.36
43	79	68	53.76	47.04
44	99	92	47.04	33.60
45	68	72	33.60	38.08
46	93	95	56.00	62.72
47	76	74	51.52	47.71
48	114	93	53.70	49.28
49	111	98	51.96	56.00
50	69	61	49.08	44.80
Average	99	100.4	51.13	49.72

Our findings give us reason to believe that if a pregnant woman's blood sugar level is low, the blood sugar level in her baby will almost

always be as low, or lower. It also appears to be a fact that the alkali reserve figures in mother and baby at delivery will approximate each other.

These investigations were undertaken to determine whether or not hypoglycemia contributes to the fetal and neonatal mortality. In view of the results so far obtained, we cannot avoid philosophizing concerning the cause of neonatal deaths of babies from toxemic mothers.

Eclampsia and preeclampsia are accompanied by a high fetal and neonatal mortality. The medical literature is vague as to the cause of death. In any disease characterized by a high mortality, conditions incompatible with life, which are characteristic of the disease, are found fairly constantly at necropsy. Such postmortem findings are not the rule in babies who die after birth from toxemic mothers.

Stander, Eastman and Harrison[4] have suggested that the true acidosis of eclampsia may be a factor in producing the high fetal mortality. Tunis[5] feels that prematurity is responsible, in part, for the high mortality. Tyson and Bowman[6] agree that there are more immature infants born of eclamptic mothers than of the average, and point out that in their study, the babies who survived did not regain their birth weight as rapidly as the average baby. In their study of both the eclamptic and preeclamptic groups only two babies out of 21 showed evidence at autopsy of direct damage from toxemia, and this evidence in one case consisted of acute degeneration of the liver. In the other case, focal necrosis of liver and kidneys was found. Many authors feel that an unknown toxin circulating in the mother's blood is responsible for fetal death.

The writings of Titus[7, 8, 9, 10] and his coworkers on hypoglycemia accompanying eclampsia and preeclampsia drew our attention to a consideration of the fetal blood sugar. As our experience agreed with theirs, so far as the mother was concerned, it seemed probable to us that if the mother suffered from marked hypoglycemia immediately preceding birth, the baby had a corresponding hypoglycemia. It seemed obvious that a baby born with hypoglycemia further depleted its blood sugar during the first twenty-four hours after birth, a time when little or no carbohydrate was provided in its diet; and that in some babies, the blood sugar level was lowered to a point where the hypoglycemia was incompatible with life, and death ensued. We opined that the blood sugar could drop to a fatal level without the onset of convulsions if the decrease were gradual.

Symptoms exhibited by the babies we observed which died within forty-eight hours after birth from toxemic mothers had much in common with those shown by patients with marked hypoglycemia due to overdoses of insulin, except that the course was very much slower in the infants.

We have had little experience with blood sugar levels in toxemic mothers and their babies, untreated with glucose. Our results, however, have led us to believe that a toxemic patient should be given enough glucose, in optimum concentration, to maintain her blood

sugar at a normal level. If this is done, it is reasonable to believe that her baby will be born with a blood sugar level high enough to protect it against fatal hypoglycemia.

If a toxemic mother has not received sufficient glucose to bring her blood sugar and that of the baby to a normal level, we believe that the baby should be protected by an injection of glucose into the umbilical vein at birth. This should be done prophylactically in any case where there is a suspicion of the existence of hypoglycemia. By such procedure it may be possible to lower the high neonatal mortality of eclampsia and preeclampsia.

It would be interesting to see reports on blood sugar levels of eclamptic women and their babies from clinics where many such are treated. Comparisons should be made between findings in women and babies treated with glucose and those not so treated.

SUMMARY

In a series of 100 cases it has been shown that the sugar content of the blood of a newborn baby is approximately that of its mother. This is also true of the alkali reserve, and the following figures have been established. In 100 normal private patients the blood sugar average for mothers was 100.5 mg., for babies, 95.4 mg. In 50 normal private patients the average alkali reserve for mothers was 51.13, for babies, 49.72. Neonatal death following birth from an eclamptic mother is presumably caused in many cases by hypoglycemia, because if the mother has a low blood sugar, that of the baby will be low. We also feel that it can be assumed that if the mother has a low alkali reserve, her baby will have a low alkali reserve at birth; if the mother has an acidosis, the baby will have an acidosis at birth. Prophylactic injection of glucose into the umbilical vein might save the lives of babies born of toxemic and eclamptic mothers.

We suggest that this study be carried on by those who see many cases of eclampsia.

415 Stevens Building

REFERENCES

(1) *Holman, A. W., and Mathieu, A.:* Am. J. Obst. & Gynec. **25:** 138, 1933. (2) *Osgood, E. E., and Haskins, H. D.:* Laboratory Diagnosis, Philadelphia, 1931, P. Blakiston's Son & Co., p. 291. (3) *Ibid.:* p. 296. (4) *Stander, H. J., Eastman, N. J., Harrison, Eph., Jr.:* Am. J. Obst. & Gynec. **19:** 26, 1930. (5) *Tunis, B.:* Zentralbl. f. Gynäk. **52:** 1935, 1928. (6) *Tyson, R. M., and Bowman, J. E.:* Arch. Pediat. **48:** 270, 1931. (7) *Titus, P., and Willetts, E. W.:* Am. J. Obst. & Gynec. **14:** 89, 1928. (8) *Titus, P., Dodds, P., and Willetts, E. W.:* Am. J. Obst. & Gynec. **15:** 303, 1928. (9) *Titus, P., and Willetts, E. W.:* Am. J. Obst. & Gynec. **18:** 27, 1929. (10) *Titus, P., and Willetts, E. W.:* Am. J. Obst. & Gynec. **19:** 16, 1930.

TUMORS OF THE URETHRA

CLOVIS H. PHILLIPS, M.D., AND MARION D. DOUGLASS, M.D., F.A.C.S.,
CLEVELAND, OHIO

(From the Department of Obstetrics and Gynecology of the Western Reserve University School of Medicine and the Lakeside Hospital)

TRUE neoplasms of the urethra are comparatively infrequent. The vascular caruncle, while well known, is also clinically comparatively rare, and its descriptions are somewhat scanty. Among the benign tumors, caruncle is perhaps the most common. Fibromatous tumors of the urethra are infrequently described, as is true sarcoma. Carcinoma of the urethra is also uncommon, less than 100 cases having been reported. We wish to describe briefly examples of several varieties of urethral neoplasms in the female.

Urethral caruncles or papilliform angiomas are polypoid overgrowths of mucosa of the vestibule. They are red, small, vascular tumors and characteristic of them is their exquisite tenderness. They are usually quite small and may be sessile or pedunculated, but are rarely multiple. The true caruncle is covered with squamous epithelium microscopically, and usually is infiltrated with round cells. As Graves points out, the epithelium often points inward into the deeper tissue which on section may resemble carcinoma. The appearance and arrangement of such cells is usually so regular and uniform that a diagnosis of benignity may be easily made. Caruncles possess extreme tenderness usually noted on urination, completely out of proportion to size or appearance. That they contain an abnormal number of nerve fibers has never been demonstrated, and there is no patent reason for the irritability which is often so striking. Surgical removal of extensive caruncles is difficult and occurrence is quite common. High frequency current is usually the best treatment. The tendency toward recurrence in caruncles and the possibility of their recurrence with metaplastic changes, is noteworthy. They possess a definite tendency to recur following ill-advised or insufficient treatment as hemangiomatous lesions, which often extend locally. It is generally recognized that neoplastic change may be initiated by preceding inflammation or as a result of chemical and mechanical injury. The following case is typical:

CASE 1.—K. B., No. 22014. This patient is a white female of sixty-five years who entered the hospital complaining of dysuria of from five to six years' duration. Her symptoms had been more severe during the past year and for three months some bloody urethral discharge had been present. Several months prior to admission, the urethral lesion had been cauterized. Examination showed a small red tumor about 1 cm. in diameter protruding from the external urinary

meatus. The tumor was excised and histologic diagnosis of urethral caruncle exhibiting atypical hyperplasia was made. The lesion was considered slightly suspicious of malignant change and 350 millicurie hours of radium emanation were applied to the base. For several months the patient's condition greatly improved. She returned to the hospital after a year, with a round firm tumor 2.5 cm. in diameter. This encircled the urethra at its orifice. The patient was complaining of burning on urination and spotting. The tumor was widely excised and found to consist of greatly distended blood vascular spaces which approximated one another so closely that there was very little intervascular stroma (Fig. 1). Growing into these cavernous vessels were polypoid masses of capillary buds. A number of blood vessels were thrombosed. The diagnosis of hemangioma was made, although the peripheral portion of the tumor was the seat of subacute inflammation. Examination of the original lesion was an inflammatory mucosal polyp with no structural features suggesting primary hemangiomatous tumor. The

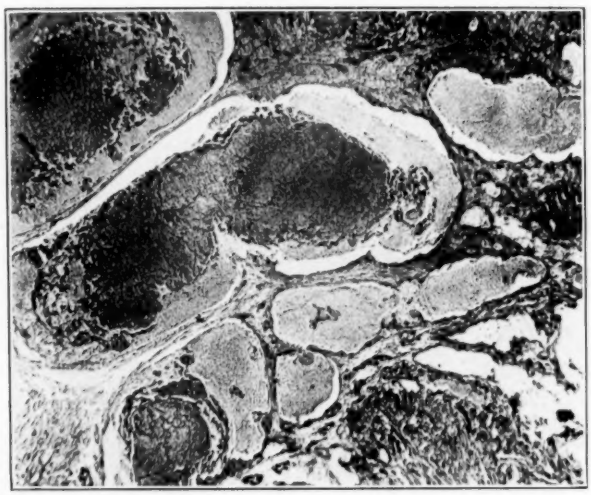


Fig. 1.—Hemangiomatous tumor representing recurrence following radiation of a urethral caruncle. Biopsy of the original lesion had shown atypical hyperplasia.

recurrence of this lesion within a year exhibited a quite different histologic picture. Follow-up on this patient revealed complete healing one year later.

All caruncles are, however, essentially vascular as described by Skene, who, in one of the earliest histologic descriptions, called them papillary polypoid angiomas. They are associated with and are often preceded by inflammation but they have frequently become frankly hemangiomatous neoplasms, especially if they recur and are apparently, at least, locally malignant.

CASE 2.—M. S., No. 16203. This case may be characterized as a hard papilloma. The patient was a while female of fifty-two years, complaining of burning on urination, nocturia, and polyuria for about two months. She had at that time noticed a small lump growing about the external urinary meatus. Examination revealed a large fibrous growth about 3 cm. in diameter attached to the left posterior edge of the urethra just inside the orifice. There was considerable local irritation about the urethra. Pelvic examination was otherwise negative. The growth, which seemed firm and fibrous, was removed with electrocautery. The sections showed hyperplasia of squamous cells which projected as papillary processes (Fig. 2). In the center of some of these processes there are focal areas

of keratinization. There is very little stroma and the epithelial cells are fairly regular in size, shape, and staining qualities, those at the base being more darkly staining. There are only a few mitotic figures. The tumor seemed histologically benign. Examination a year later revealed a normal urethra.

Fig. 2.—Squamous-cell papilloma of the urethra. Consists almost entirely of epithelial cells and is histologically benign.

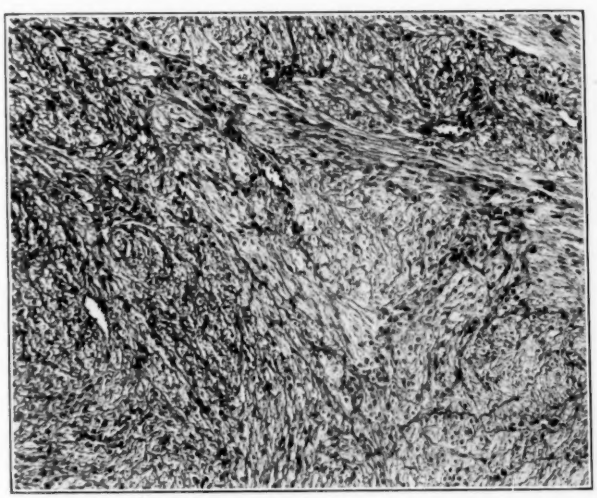


Fig. 3.—Submucous fibroma of the wall of the urethra showing very cellular structure.

FIBROMAS

Fibromas of the urethra are rare tumors. Their characteristics have much in common with myofibromas elsewhere. This case is a typical example.

CASE 3.—M. D. This patient, a white woman forty-seven years old, entered the hospital complaining of swelling of the vulva. There were no other symptoms. Examination revealed a mass 2.5 cm. in diameter lying directly beneath the urethra which was firm but not movable. Both the urethral and vaginal mucosa were intact. A vertical incision was made extending back over the urethral mucosa over this tumor which was found to have an adherent solid base on the

posterior wall of the urethra to the left side. It measured 4 by 3 by 2 cm., was elastically solid, and slightly softened in the center. Section showed edema and marked degenerative changes with the cells lying in vacuoles. There was a homogeneous acidophilic matrix almost simulating cartilage in areas (Fig. 3). Sections from the edge of the tumor showed it to be very cellular, there being irregularly disposed spindle-shaped cells of various sizes. In other places there were interlacing bundles of cells separated from each other by edematous stroma. There was no vascular invasion. There was considerable nuclear variation but very few mitotic figures. There was no well-defined capsule. Follow-up of this patient revealed normal urethra one year later.

CARCINOMA

As had been stated, carcinoma of the urethra is a rare disease but it is probably more frequent than supposed, owing to the fact that unless seen very early it is often impossible to determine whether it originated in the urethra or in some adjacent structure. The point of origin is usually stated to be at the urethral orifice from a urethral caruncle or from Skene's glands. In extension, it may be either inverting or everting in type. In the former type, it tends to spread along the para-urethral plane toward the bladder and produces a characteristic hard nodular tumor and does not invade the vaginal mucosa at first. The everting or external form is, in our experience, the more common. The tumor appears at the orifice in the first place, later involving the para-urethral tissue as in the first type. Crossen states that metastases occur in the pelvic lymph nodes and usually occur early. The first symptoms are usually dysuria, frequency, and hematuria. Pain occurs later. Radical operation may be combined with radium. Radium is the alternative treatment and has been, in the 2 cases here reported, unsatisfactory. Carcinoma of the urethra is rare before the age of fifty. Leucoplakia and caruncles are usually the forerunners. There seem to be definitely, from a clinical side, two types of carcinomas in the female urethra; the first type beginning in the mucosa, the floor of the urethra and its distal portion, and the second, a para-urethral indurated tumor tending to surround and occlude the urethra. The first type is a very malignant type, the second, slow-growing and occurs with fibrosis and hyalinization.

CASE 4.—L. W., a white woman, forty-four years of age, was admitted to the hospital complaining of slight bloody vaginal discharge. Examination revealed a mass 2 cm. in diameter and 5 cm. in length, beginning at the external urethral orifice and extending backward about the canal between the urethra and anterior vaginal wall. The posterior aspect was discolored as though it might be a tumor breaking through the mucosa. It was thought possible that bleeding had occurred from this point. Pelvic examination was normal. Cystoscopy revealed no break in the mucous membrane, and biopsy was taken (Fig. 4). Excision was attempted after the diagnosis of carcinoma simplex was made but was unsuccessful. Radium seeds were implanted about the base of the tumor. Histologic examination showed cellular tissue made up of polyhedral cells, arranged in the form of broad anastomosing cords on a scanty fibrous connective tissue stroma. The stroma tended to occupy the centers of these cords. Mitotic figures were present but were not

numerous. The cells were polymorphous, ranging from large vesicular cells to atypical spindle cells. There were areas of hemorrhage. This patient died in four months of recurrence and metastases.

CASE 5.—This patient, about fifty years old, entered the hospital complaining of pain in the lower abdomen. Physical examination was essentially negative. Pelvic examination revealed a small mass 1.5 cm. in diameter projecting from the lower margin of the external urinary meatus, which bled very easily upon manipu-

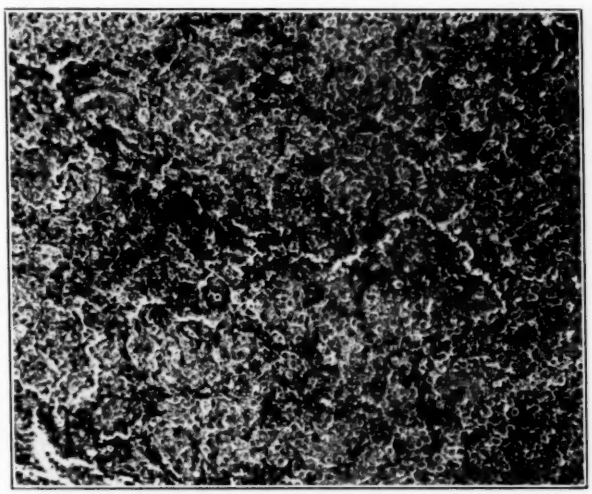


Fig. 4.—Carcinoma of the urethra originating apparently at the base of the mucosa. Treated unsuccessfully with radium.

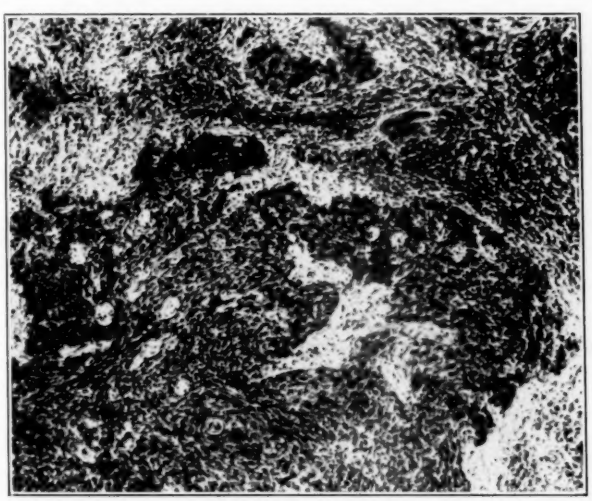


Fig. 5.—Carcinoma of the urethra originating at the urethral orifice, characterized by early bleeding. Local excision with death from pelvic metastases.

lation. This tumor was excised locally. Histologic examination showed transitional cell carcinoma (Fig. 5). Microscopic examination showed a fibrous connective tissue infiltrated by many leucocytes and somewhat degenerated. In one aspect a fairly normal epithelium of the squamous type appeared infiltrated with many leucocytes. Throughout the stroma were masses of epithelioid cells, large

and irregular with irregular nuclei, some nuclei were vesicular, others dark, and in some there were karyokynesis. These cell masses appeared to have an irregular glandular arrangement. Mitotic figures, however, were few. Follow-up on this patient revealed that she died of pelvic metastases in about a year.

In the treatment of carcinoma of the urethra, early diagnosis is extremely important because metastases take place early. Following the diagnosis of carcinoma, if surgery is to be attempted, a radical resection of the entire urethra is the only possibility of cure. Early operation has often been avoided because adequate surgery is so often followed by incontinence of urine.

The following plan recommended by Crossen is of importance: A vesicovaginal stab wound is made into the bladder into which a catheter may be placed. This is to be well back in the region of the trigone away from the vesical neck. The urethra is completely excised down to the neck of the bladder. It is necessary to fill the defect and at the same time by a purse-string suture about the vesical neck to attempt to secure continence. This may be done by sliding vaginal flaps in favorable cases. Following complete resection of the urethra with complete destruction of the urethral sphincter, it is sometimes possible by transplantation of levator muscles to secure continence.

SUMMARY

Urethral caruncles of the vascular type tend toward recurrence and when they do recur, may reappear as hemangiomatous tumors which are difficult to eradicate and are locally malignant.

The presence of chronic infections or caruncles seems to be the precursor of urethral neoplasms.

Early diagnosis of carcinoma of the urethra is of the greatest importance because otherwise operative treatment is extremely unsatisfactory.

Radical surgery followed by adequate plastic procedure offers the only desirable treatment for carcinoma of the urethra. Radium is difficult to apply and is extremely likely to cause incurable vesico-vaginal fistula. Surgical excision, if possible, is the treatment of choice.

REFERENCES

(1) *Crossen, H. S.:* Tr. Am. Gynec. Soc. **40:** 111-126, 1915. (2) *McMurtry, L. S.:* Ann. Surg. **47:** 1032, 1908. (3) *O'Neill, R. F.:* J. Urol. **5:** 343, 1921. (4) *Percy, J. F.:* Am. J. Obst. **47:** 457-483, 1903. (5) *Pugh, W. S.:* AM. J. OBST. & GYNEC. **14:** 57-62, 1927. (6) *Scholl, A. J. Jr., and Brash, W. F.:* Ann. Surg. **76:** 246-259, 1922. (7) *Venot, A., and Parcelier, A.:* Rev. de Chir. Paris **59:** 471-475, 1921.

THE TREATMENT OF RECENT PUERPERAL INVERSION OF THE UTERUS, WITH A REPORT OF FIVE CASES

(From the Department of Gynecology and Obstetrics of the University and Bellevue Hospital Medical College of New York University)

DAVID NYE BARROWS, M.D., F.A.C.S., NEW YORK, N. Y.

FORTUNATELY for obstetricians, the frequency of uncomplicated puerperal inversion of the uterus is sufficiently low to keep this tragic accident from occurring much more than once or twice in the experience of most physicians. We have observed five cases, followed their course closely, and feel that several valuable conclusions can be drawn from the variations in course and treatment of this series. These cases all came under observation within a short period after the inversion had occurred; for that reason the discussion will be confined to this recent type of case and any mention of the so-called chronic type will be omitted, which is often seen at long intervals after its occurrence.

CASE 1.—Mrs. B. S., aged eighteen. Admitted to the Gynecological Service at Bellevue Hospital, Feb. 25, 1924, complaining of vaginal bleeding.

She gave a history of an easy labor of seven hours' duration in a hospital two and one-half months previously. Her puerperium was reported as stormy necessitating two blood transfusions.

Two months postpartum she bled profusely for about two hours, passing numerous clots. At a hospital in Jersey City, she was found to have a complete inversion of the uterus and an attempted replacement there was unsuccessful.

Our examination on admission disclosed a grey shaggy mass filling the vagina. This was globular, 4 cm. in diameter, with a small portion of the cervical ring still palpable posteriorly. No fundus could be made out separate from this mass.

The surface appearance of the mass was suspicious looking, but a culture for Klebs-Loeffler was made, which proved negative.

Under douches, tampons, and transfusions, she improved steadily in general health and (on March 8, 1924) two weeks after admission, the sloughing appearance had cleared up, but there was still a profuse discharge.

On March 14, three weeks after admission, during which time she had been kept in the elevated foot position, she was examined to see if she were ready for operation, when it was discovered that the fundus was no longer inverted but was normal in size and retroverted. One month later (April 17, 1924) she was found to have a slightly relaxed parous introitus; firm, lacerated cervix, admitting a finger tip; fundus retroverted, anteflexed, 5 cm. long and about 4 cm. wide, being freely movable with no palpable adnexal pathology.

She was then referred to the clinic for ambulatory observation and was followed for four months.

This case history is an excellent example of how unexpectedly an inverted uterus may replace itself.

CASE 2.—M. K., aged twenty-five, para iii, admitted to the Obstetrical Service, Bellevue Hospital, July 8, 1925 at the School for Midwifery. With her last previous

confinement in 1924 in Bellevue she had a retained placenta succenturiata with profuse hemorrhage. She delivered spontaneously on July 9, 1925, at 1:35 A.M., of a full-term child. No effort was made to express the placenta until 2 A.M., (twenty-five minutes later), when the amount of pressure used may have been excessive and, although "nobody pulled on the cord," the whole inverted uterus with placenta and membranes still attached, appeared between the patient's thighs. She was described as being "in extremis, pulseless, with breathing very shallow and rapid, lying in a huge lake of blood." Treatment for shock was immediately instituted.

After she had rallied, the placenta was removed from its attachment to the uterus with *extreme difficulty* as though its attachment were purely fibrous.

The uterus was pushed back into the vagina but the inversion was not overcome in spite of a serious effort. The vagina was then packed. After ten days a Spinelli operation was performed. The postoperative reaction was considerable. In spite of repeated transfusions her convalescence was delayed by the development of a pelvic hematoma, a small pulmonary embolism and a moderate thrombophlebitis of the right femoral vein. She was discharged on the thirty-fifth day postoperative in satisfactory condition.

The most interesting part of her record follows:

The patient was carefully instructed to report to the Obstetrical Department promptly, should she again become pregnant but was not seen until readmitted Oct. 9, 1927, two years later in active labor. She was watched carefully for any signs of rupture of her uterus and delivered a stillbirth the following day, after twelve and one-half hours of moderate labor. Delivery was easy and no Credé maneuver was employed, as the placenta delivered spontaneously and appeared intact.

However, she had had severe pains over the left side of the uterus throughout labor, and though this was relieved by morphine, she complained later and continuously of tenderness over her left lower abdomen.

About three hours postpartum, the patient suddenly went into shock, pulse 160, respiration 42. There was no vaginal bleeding. About four hours later she was examined vaginally by one of the visiting obstetricians who felt a rupture in the anterior uterine wall. She was then transferred to the Gynecological Service and a rapid hysterectomy was performed by Doctor Holden. The uterus was found ruptured through the upper half of the Spinelli scar. She was given several transfusions and other supportive treatment but died eight days after operation. Autopsy showed lobular pneumonia of both lungs and marked adhesive peritonitis with a rupture of the uterine wall, through scar tissue, areas of calcification showing evidence of old infection of the scar following the Spinelli operation.

This case brings out the principal objections to the end-results of the Spinelli procedure:

1. The resulting weak uterine wall, with great tendency to rupture if subsequent labor occurs.

2. The healing of the muscular wall by third intention as shown by calcified areas in the uterine wall.

CASE 3.—Mrs. E. B., aged sixteen, para i, born in United States of Italian parents; was admitted to the Gynecological Ward at Bellevue Hospital, on Dec. 26, 1925. Her chief complaint was vaginal bleeding of one month's duration ever since delivery by a midwife. She was found to have a complete inversion of the uterus and five weeks after admission her general condition was felt to be satisfactory for a Spinelli operation. This was done with moderate postoperative morbidity. Three weeks postoperative, the examination revealed the fundus small, anterior and freely movable,

with no palpable adnexal pathology. She left the hospital five days later, twenty-six days postoperative in good condition, with a red count of 3,000,000 and hemoglobin of about 55 per cent.

This patient was followed for four and one-half years up to which time she had not become pregnant, as she had been using contraceptive measures. Her pelvic examination was negative throughout except for a slight tendency to retroversion.

This result is satisfactory to date. From our subsequent experience, we would now approach such a problem by the abdominal route. We might have been able to reinvert this uterus intact without leaving any scar or at least, one stronger than that of a Spinelli operation.

CASE 4.—Mrs. M. P., aged thirty-four, admitted to the Obstetrical Service of Bellevue, Sept. 24, 1930.

She was brought to the hospital in shock, with a history of postpartum hemorrhage, following a two-day labor, at full term with her second pregnancy. The third stage had lasted forty-five minutes, when a Credé expression of the placenta was attempted, accompanied by moderate tension on the cord. With considerable loss of blood, the patient went into collapse. This was profound when she reached the hospital and her blood pressure was recorded as 50 over zero. She was treated first and foremost for shock, temporarily neglecting the uterine inversion which was present.

About five and one-half weeks postpartum she was in condition for operation. In the interim she had received locally hot permanganate douches, mercurochrome instillations, and daily glycerin vaginal packing which is our routine. Laparotomy revealed the typical appearance of a completely inverted uterus which was well involuted. This was grasped in the hand like a collapsed rubber ball. Pressure on the lower end with slight anteroposterior compression caused the uterus to slip back into its normal position with almost miraculous ease. This broke up a few fibrous adhesions of the serous coat whose slight oozing was easily controlled by a hot compress. A one point suspension with No. 1 chromic catgut was the only procedure before closing the abdomen, as the circulation in the fundus appeared to be reestablished normally in short order.

This patient was followed in the clinic for six months during which time her menstruation became normal and she apparently has been in perfect health.

This procedure, we believe to be the method of choice, leaving as it does a practically unimpaired uterine musculature.

It is quite true that some cases will not be so readily amenable to reinversion. Pressure can be also applied to the fundus from below by a sponge stick in the vagina but occasionally a case will be encountered where even this additional aid with traction from within the collapsed uterus by clamps, etc., will all prove of no avail.

A simple procedure which will take care of such a problem quite readily is well illustrated by a case seen by me in consultation and subsequently operated upon with a very pleasing result.

CASE 5.—A healthy twenty-four-year-old primiparous patient whose uterus had inverted immediately after the third stage of an otherwise uneventful spontaneous delivery under excellent supervision, was seen in April, 1930, two days postpartum. She had one transfusion, but was unable to get more, so that her subsequent convalescence was delayed.

About ten weeks postpartum her general condition permitted operation. Laparotomy revealed a well involuted completely inverted uterus in healthy condition.

No response to compression from below, even with the aid of a sponge stick in the vagina, directed by the abdominal hand and a finger in the pouch of Douglas

after the method of Irving and Kellogg or traction by clamps was of any avail, so that an adaptation of the Spinelli procedure was resorted to.

The vaginal wall and cervical ring being almost on the level of the symphysis pubis anteriorly due to the position of the uterus in the vagina, this had allowed the rectal wall to fall away a little posteriorly.

The posterior cervical lip, where covered by posterior vaginal wall and peritoneum was incised in the middle line, the incision being carried down to the fundus. This being easily accomplished, the fundus was turned right side out without difficulty as in the Spinelli and Schroeder vaginal operations.

The uterine incision was closed by interrupted chromic sutures and the fundus secured in position by an Olshausen shortening of the round ligaments. Recovery was uneventful, the patient going home on the twelfth postoperative day. She has been in excellent condition since. She was instructed to employ contraceptive measures.

This operative procedure proved to be extremely simple and easy, and in very marked contrast to the technically and mechanically difficult vaginal operations, i.e., Spinelli, Schroeder or vaginal hysterectomy. It also has left the patient with a scar which should be at least as strong as or stronger than when done from below.

At the time of operation, this patient had a red blood count of only 3,500,000 with hemoglobin of 60 per cent, and convalesced very rapidly, showing how little shock was involved.

She last reported in December, 1932, that she was in excellent health.

This method is not as satisfactory as that employed in Case 4, but we feel it has a much broader field, even though it does not leave an entirely undamaged uterine muscle wall.

CONCLUSIONS

1. Immediate replacement of puerperal uterine inversion is frequently attended by considerable shock and loss of blood, and is a dangerous procedure.

2. The prompt treatment of shock is much more important than attempting to replace the uterus when the patient is in doubtful condition.

We even go so far as to advise packing to stop hemorrhage before removing the adherent placenta.

3. The vaginal operations for replacement are difficult, tedious, and dangerous and at best leave a scarred uterine muscle wall.

4. The abdominal operation at from four to twelve weeks postpartum is simple and free from shock, and if done when the uterus is sufficiently pliable, can give an ideal result; i.e., uterus unscarred in normal position which may be suspended to prevent recurrence. Coincident sterilization is simple if that is deemed advisable.

5. We prefer not to deliver a woman per vaginan who has had a Spinelli, Schroeder, or similar operation but advise an abdominal cesarean section before the onset of labor.

6. We think of the acute case in terms of shock and not in terms of inversion of the uterus.

130 EAST FIFTY-SIXTH STREET

NEMBUTAL AND SCOPOLAMINE ANALGESIA IN LABOR, WITH A REPORT OF 160 CASES*

LEONARD AVERETT, M.D., F.A.C.S., PHILADELPHIA, PA.

THE ideal procedure for obstetric analgesia should combine, first, a maximum degree of safety both to mother and child; second, a decided relief from pain; third, no interference with the contractility of the uterine musculature, which must be maintained in order to assure the progress of labor and thus obviate the dangers of postpartum hemorrhage; and fourth, it must also be easily administered.

Most of the methods have been found wanting. The usefulness of chloroform and ether, for instance, is limited to the end of the second stage; with them, there is practically no stage of amnesia and they may temporarily stop uterine contractions. Chloroform is definitely toxic in the presence of liver and kidney disease. Colonic ether is generally uncertain in action, occasionally irritating to the intestinal mucosa and has not been widely accepted. Morphine and scopolamine combinations are satisfactory only during the first stage and have no place during the second and more painful stage of labor, as the effect must be expended before the delivery of the child is contemplated. Nitrous oxide and oxygen anesthesia, although yielding excellent maternal and fetal results, become prohibitive in price if given for any prolonged period, and requires the assistance of a trained anesthetist.

The more recent literature contains many reports on the use of barbituric acid derivatives, alone, and in combination with other drugs for analgesia in labor. The absorption of the barbiturates is very rapid and elimination, occurring through the kidney and liver, is extremely slow; and for this reason, one must take into serious consideration the possibility of the cumulative action of any barbiturate. The toxicity of some of those compounds is apparently in inverse proportion to the rate of elimination, but, unfortunately, their rates of elimination have as yet not been definitely determined. This, however, does not hold true with nembutal (penta-barbital sodium), which is excreted much more rapidly than pernocton and sodium amytal, and is, therefore, much less toxic. Our results with the use of nembutal, in combination with scopolamine, the latter prolonging the action of the former, in the series of cases here reported, would seem to prove its efficiency in obtaining safe obstetric analgesia.

We found that nembutal (penta-barbital sodium) has a profound sedative but shorter hypnotic action, causes much less restlessness than

*Read at stated meeting of the Obstetrical Society of Philadelphia, May 4, 1933.

sodium amytal or pernocton, and its action is readily prolonged by the addition of scopolamine. We experimented with various doses and finally came to the conclusion that the best results were obtained in the average case by the oral administration of 6 gr. of nembutal, made up into four capsules, 1½ gr. each, at one time. Scopolamine hydrobromide, grains $\frac{1}{100}$, is administered hypodermatically when labor is definitely established, with satisfactory uterine contractions at least every five minutes, and when the cervix is partially effaced and two fingers' dilated. The average duration of analgesia during labor was five and one-half hours. The above dosage was used in 160 cases. Only in 28 primiparous and 2 multiparous patients was additional medication administered, usually 3 gr. of nembutal and $\frac{1}{150}$ grain of scopolamine. The average duration of amnesia following labor was two hours. Nitrous oxide and oxygen was administered at the end of the second stage of labor in all cases.

The clinical effect of the drugs is drowsiness, followed in fifteen to thirty minutes by profound sleep. Some patients awakened from time to time with the pains, others were only partially aroused, while a few did not move at all as pains appeared. Some patients could be aroused easily and talked and answered simple questions, while others were aroused only with great difficulty, answered questions very slowly and dropped back to sleep during questioning. Another group of patients could not be aroused sufficiently to answer any questions while a small number, although not awake, were rather noisy during labor pains.

There was no change noted in the respiratory rate; in only a few cases was the pulse rate slightly increased; the blood pressure generally dropped from 5 to 10 mm. The pupils were moderately dilated; conjunctival and corneal reflexes were absent in several of our patients; no nystagmus or diplopia was noted.

The frequency and severity of uterine contractions were not interfered with. The first stage of labor was unusually rapid in some cases, most likely due to the sudden relaxation and dilatation of the lower uterine segment. The second stage of labor also progressed normally. There was no prolongation of the third stage noted. Postpartum hemorrhage occurred in only one case and necessitated uterine packing. This happened in a multipara who had a spontaneous delivery of a child weighing ten pounds and a large quantity of amniotic fluid.

Of the 160 cases studied in this series, 126 were primiparas and 34 multiparas. The average length of labor of the primiparous patients, after entering the hospital, was nine and one-half hours; the average length in the case of the multiparous patients five hours and ten minutes.

Types of Delivery.—There were 25 spontaneous deliveries; 119 patients were delivered by perineal forceps and lateral episiotomy was performed; there were 12 midforceps, 2 breech deliveries with forceps

used on the after-coming head in one; 2 cesarean sections were performed in borderline cases after a test of labor. We delivered almost all of our primiparas by perineal forceps and accompanying episiotomies. The advantages of this procedure are well known and need no explanation.

Our conclusions as to the effectiveness of nembutal and scopolamine, as a method of obstetric analgesia in the 160 cases hereby reported, are based upon the statements of the patients themselves, when questioned by us, the day after delivery. In 110 cases, the patients experienced complete amnesia after medication was administered. In 42 cases, the patients had some recollection of a few incidents during labor, but very little recollection of pain. In only 8 cases was complete failure experienced. These patients, all multiparas, were well advanced in labor upon admission to the hospital and were delivered in from one to one and a half hours after the medication was given.

There was no maternal or fetal mortality in the entire series and 152 babies either breathed or cried immediately after delivery; 8 required mild resuscitation; of these, three had been delivered by mid-forceps and one was a breech delivery with forceps used on the after-coming head.

2106 Spruce Street

DISCUSSION

DR. CLIFFORD B. LULL.—I desire to endorse the statements of Dr. Averett and believe that we must separate analgesia from anesthesia. Ether, chloroform, and other anesthetics should be left out of a discussion of this kind.

I have completed a series of cases on Dr. Vaux's service at the Lying-In Hospital in which half the cases have received a barbiturate with ether by bowel and the other half nembutal with scopolamine. There were a total of 265 cases in this series and I can sum up our results by saying that having tried Gwathmey's technic, in which only 51 per cent were successful, and use of various other analgesics, I personally believe that the last 150 cases given nembutal and scopolamine were the most satisfactory. The nembutal was given by mouth in the approximate dose of 6 gr. and the scopolamine in a dosage of 1/150 or 1/200. I do not believe that the routine dosage should be the same for every patient, as we have found that the smaller dosage is sufficient in some cases, and also that in some cases it is not necessary to follow the nembutal with the scopolamine.

After reviewing the results of several hundred cases of several analgesics, I feel that there should be no routine analgesia administered to a woman in labor. Every patient should be given an analgesic, but it should be selected for every individual patient.

Another point in using this form of analgesics should be impressed upon the general practitioner or anyone doing obstetric work in the home. These patients are very frequently so amnesic from the use of these drugs that they will not cooperate during the second stage of labor, and therefore it becomes necessary in a very high percentage of cases, to terminate the second stage of labor by the use of outlet forceps.

I wish also to call attention to the fact that these drugs aid in the dilatation of the cervix and very often result in a rather precipitous delivery.

And finally, after reviewing my experience with various drugs given in the first and second stages of labor, I am firmly convinced that the day is fast approaching when we will no longer use morphine during the late first or second stages of labor. In our last series using nembutal and scopolamine there was no baby narcotized and there was no patient who had a postpartum hemorrhage.

PATHOGENICITY OF THE MONILIA (CASTELLANI), VAGINITIS AND ORAL THRUSH

H. C. Hesseltine, M.D., I. C. Borts, M.D., and E. D. Plass, M.D., Chicago, Ill., and Iowa City, Iowa

(From the Department of Obstetrics and Gynecology and the Department of Hygiene and Preventive Medicine, State University of Iowa)

IN TWO previous communications,[1, 2] it has been pointed out that fungi of the monilia* (Castellani) group are frequently associated with definite vaginitis, and that pregnancy and diabetes are predisposing factors. Moreover, it has been postulated that oral thrush in newborn infants may be due to natal or postnatal contamination by maternal vaginal discharges containing the causative organisms. However, no evidence was offered to show that the monilia are pathogenic in the vagina, nor that the vaginal organisms can produce oral thrush when inoculated into babies' mouths. It is the purpose of this report to summarize the evidence we have gained from human inoculations in support of our previous hypotheses.

VAGINITIS

The only reference in the available literature to successful human vaginal inoculations with fungi is that of Haussmann,[3] who transferred the vaginal discharge of a patient with mycotic vaginitis directly to the fungus-free vagina of a normal pregnant woman. Several days later vaginal burning and itching were noted, but subsided spontaneously within a short period. In other instances, this investigator was unable to reproduce this result with material from other sources. These experiments were inconclusive since pure cultures were not employed and the action of associated organisms could not be excluded.

By colony isolation on Sabouraud's plates, we secured pure cultures of monilia from various sources, and identified them according to Castellani's classification. Single loopfuls of forty-eight-hour cultures

*We have considerable evidence to show that the organisms concerned are endomyces rather than monilia, since they develop asci under proper cultural conditions.

of these fungi were distributed well along the vaginal walls of 31 women, whose vaginal discharges were shown by culture to be fungus-free immediately preceding the experiments. Nine of these patients were not pregnant but had been admitted to the clinic for pelvic complaints other than vaginitis or leucorrhea, while 22 were in the last trimester of normal pregnancies. An inoculation was designated "successful" only when a clinical vulvovaginitis developed, and the uninformed patient voluntarily complained of local symptoms. Using such criteria, the results obtained with various types of the organism are given in Table I. The Saccharomyces cerevisiae (baker's yeast) was utilized as a control under exactly comparable conditions.

TABLE I. VAGINAL INOCULATIONS

The Fungi Are Classified According to Castellani

TYPE OF MONILIA	INOCULATIONS	SUCCESSFUL RESULTS
Pregnant		
Monilia pinoyi	6	6
Monilia metalondinensis	3	3
Unclassified No. 120	10	4
Unclassified No. 139	3	2
Saccharomyces cerevisiae	10	0
Nonpregnant		
Monilia pinoyi	9	6
Saccharomyces cerevisiae	3	0

Early symptoms (local heat, swelling, dryness, itching) appeared never before twelve nor later than seventy-two hours after inoculation. An increased discharge frequently followed twelve to twenty-four hours after the initial symptoms, together with smarting, burning, and general vulval soreness. In the early stages, the vulval and vaginal mucous membranes appeared dry and reddened, while later they became injected, tender, and slightly edematous. Occasionally, small excoriated areas or scattered, white, thrushlike patches developed (Fig. 1). At the height of the infection, the appearance was that of a mycotic vaginitis of moderate severity.

After inoculation, repeated cultures were made and subcultures proved the recovered organism to be identical with the organism used for the inoculation. Among the nonpregnant group, the experimental infection was definitely self-limiting, and was followed to complete spontaneous disappearance of the fungi. On the other hand, among the pregnant women the infection was more persistent, but in only a few instances was active treatment necessary. No untoward symptoms, other than moderate discomfort, followed any of the inoculations. This tendency of the experimental lesions to be of little consequence accords with the observations of Dowling,[4] who determined the pathogenicity of monilia and other yeastlike fungi on the skin and

wrote: "The artificial lesion is of short duration," and "Their pathogenicity is of low-grade order, the degree of reaction being dependent as much on the soil as on inherent virulence."

ORAL THRUSH OF THE NEWBORN

The suggestion has been offered from time to time that oral thrush of the newborn may be due, at least occasionally, to contamination of the infant's mouth with the causative fungus present in the vaginal discharge of its mother at or shortly after delivery.

Fig. 1.—Experimental vaginal moniliasis.

Haussmann[3] demonstrated fungus spores immediately after birth in the mouths of children born from mothers whose vaginal discharges harbored the organisms at the time of parturition. Even though none of these children developed clinical oral thrush, this investigator expressed the conviction that this mode of infection was probable and that it was advisable to treat the maternal vaginal infection, even if it produced no discomfort, as a protection for the newborn. ("..., par l'élimination des spores et du mycôsis une fois dévelope durant la grossesse et par la plus grande propreté pendant l'accouchement, peut être radicalment coupée une source du muguet . . .") Noack[5] quotes Veit as having observed a case of oral thrush in an infant born of a mother who had mycotic vaginitis, and holds that direct contamination at birth may well account for certain cases of thrush. Faber and Clark[6] and Cron[7] have more recently noted this association, the former saying, "It is highly advisable that the obstetrician watch for signs of thrush in the mother, and, finding them, advise isolation of the baby," while the latter author says: "Vaginal moniliasis may be transmitted to the newborn and at an early date may appear in the mouth of the infant as thrush. It is therefore essential that the mother be relieved of the presence of this fungus before the onset of labor."

The constant association of monilia (Castellani) with oral thrush has established this fungus as the causative agent, but we can find no evidence that experimental proof has ever been offered through direct inoculation with pure cultures of the organism. Such experimental data were necessary to prove conclusively that the fungi present in the vaginas of pregnant women could produce oral thrush in their newborn children. Accordingly, pure cultures of the monilia (Castellani) from various sources and representing different strains, as determined by their cultural reactions, were inoculated directly into the fungus-

Fig. 2.—Experimental oral thrush.

free buccal cavities of healthy newborn children less than one week of age. The criterion for successful inoculation was the appearance of typical clinical thrush. Photographic evidence of the condition was obtained, after which treatment with 1 per cent aqueous gentian violet solution was instituted until mouth cultures were negative for the fungus. When the lesion was well developed, cultures were obtained and the fungus isolated from plates was shown by its reactions in carbohydrate media to be identical with that employed for the inoculation. No harmful effects were noted. Table II indicates the results obtained in 29 babies with six types of monilia and with the Saccharomyces cerevisiae (baker's yeast) used as a control.

TABLE II. ORAL INOCULATIONS

The Fungi Are Classified According to Castellani

TYPE OF MONILIA	INOCULATIONS	SUCCESSFUL RESULTS
Monilia pinoyi	7	7
Monilia krusei	5	0
Unclassified No. 3	3	1
Unclassified No. 4	2	0
Unclassified No. 120	5	1
Unclassified No. 182	2	0
Saccharomyces cerevisiae	5	0

In this limited number of experiments, three apparently different strains produced typical lesions, but only a single type (Monilia pinoyi, Castellani) gave repeated successes. The observation that several types of monilia (Castellani) may produce oral thrush agrees with Castellani's results.[8]

CONCLUSIONS

The causal relationship of certain fungi of the monilia (Castellani) group to vaginitis and to oral thrush has been demonstrated and Koch's postulates have been satisfied.

Monilia obtained from the vaginas of pregnant women can produce oral thrush in newborn children. Direct contamination of the mouth with the vaginal discharges during or shortly after birth offers an acceptable explanation for certain sporadic cases of thrush.

REFERENCES

(1) *Plass, E. D., Borts, I. H., and Hesseltine, H. C.:* J. Iowa State Med. Soc. 20: 121, 1930. (2) *Plass, E. D., Hesseltine, H. C., and Borts, I. H.:* AM. J. OBST. & GYNEC. 21: 320, 1931. (3) *Haussmann, D.:* (Translated by P. E. Walther.) Parasites des organes sexuels femelles de l'homme et de quelques animaux, avec une notice sur le développement de l'Oïdium Albicans Rob, Paris, 1875, J-B Bailliere et Fils. (4) *Dowling, G. B.:* Brit. J. Dermat. & Syph. 42: 562, 1930. (5) *Noack, F.:* Ztschr. f. Geburtsh. u. Gynäk. 72: 739, 1912. (6) *Faber, H. K., and Clark, E. B.:* Am. J. Dis. Child. 34: 408, 1927. (7) *Cron, R. S.:* Trans. Am. Assn. Obst. Gynec. & Abd. Surg. 42: 225, 1929. (8) *Castellani, A.:* J. Trop. Med. & Hyg. 23: 17, 1920.

A COLD LIGHT FOR INSPECTION AND TRANSILLUMINATION OF THE CERVIX

SAMUEL GORDON BERKOW, M.D., PERTH AMBOY, N. J.

SUCCESSFUL use of the "cold" surgilite (Cameron) in transillumination of the breast suggested the use of a similar light in the cervix. Accordingly, a lamp was designed for this purpose, and has been made by the Cameron Surgical Specialty Company, of Chicago.

Fig. 1 shows the lamp which is 22 cm. long and 4 cm. wide, with a curved tip. The rubber acorn is adjustable and prevents the reflection of light back through the cervical os. This lamp is extremely brilliant. Prolonged use does not cause it to become more than comfortably warm. The entire lamp is boilable. With proper precautions it can be introduced beyond the internal os.

Current is supplied by batteries, or house current stepped down by the Vitrohm Potential Adjuster. Because of the brilliance of the lamp, if the latter is preferred the makers suggest using not more than three-fourths of the current that can be secured from it.

With the patient in the lithotomy position, a vaginal speculum is introduced. A black hard rubber or surgimold speculum is to be preferred. The portio and the cervical canal are cleansed. The cervical canal is painted with a germicidal

Fig. 1.

solution, tincture iodine or mercurochrome, on a cotton-tipped applicator. The length of the cervical canal is measured on this applicator. The acorn is adjusted to the proper position on the lamp. The room is darkened, but need not be very dark. Finally the lighted lamp is introduced.

Dr. I. S. Rubin has suggested the advisability of steadying the cervix with a volsellum. This aids the introduction of the lamp and improves inspection of the transilluminated cervix.

For ten weeks this lamp has been used almost daily by me, in my private practice, in the Perth Amboy General Hospital, or in the Out-Patient Department, Gynecological Service, Mount Sinai Hospital, New York City.

There has been no opportunity to test the usefulness of transillumination of the cervix in distinguishing between solid nodule and nabothian cyst. However, certain advantages of this lamp have become increasingly apparent, and these prompt the present report.

First, this lamp makes possible a better inspection of all exterior surfaces of the cervix than is obtained with a fixed light. Lesions can be inspected with the lamp at close range and turned to any desired angle.

Second, transillumination of the cervix reveals nabothian cysts clearly, no matter how deep-seated. The anterior and posterior surfaces of the cervix are inspected

separately, with the curve of the lamp in the direction of the surface to be viewed. Seen in this manner, all nabothian cysts can be destroyed by puncture with a fine electrocautery. The curve of the lamp in the cervical canal steadies the cervix while these punctures are being made.

When further data have accumulated, it is hoped that transillumination of the cervix as a diagnostic procedure will merit a detailed report.

THE INFLUENCE OF POSTURE UPON THE MOVEMENT OF FLUID IN THE TRACHEA OF THE NEWBORN

An Experimental Study

Douglas P. Murphy, M.D., Philadelphia, Pa.

(From the Gynecean Hospital Institute of Gynecologic Research, School of Medicine, University of Pennsylvania)

THE presence of amniotic fluid in the tracheas of infants asphyxiated at birth, raises the question of the effect of posture upon the movement of fluid in this location.

Observations upon the influence of posture on the movement of fluid injected into the tracheas of paralyzed cats (which were kept alive by artificial respiration in a Drinker respirator) throw some light upon this clinical question.[1]

EXPERIMENTS

The test animal was etherized, and cannulas were tied in the trachea and in the femoral vein. After being placed in a Drinker respirator, respiratory paralysis was produced by the intravenous injection of 1.5 c.c. of a 1.0 per cent watery solution of curare. The animal was kept alive for an hour by artificial respiration, employing a breathing rate of 15 per minute, and a recurring subatmospheric pressure of 10 to 15 cm. of water, alternating with atmospheric pressure.

At the start of the experiment, fluid was injected into the tracheal cannula. It consisted of the animal's heparinized blood plasma, to which a small amount of methylene blue was added. In each case, approximately 15 to 20 c.c. of the mixture were injected, over a fifteen- to twenty-minute period, coincidentally with each artificially induced inspiration.

Experiments were conducted with each animal either (1) horizontal, (2) vertical, head up, or (3) body inclined at an angle of 15 degrees with the horizontal, head down. At the end of the hour of artificial respiration, the animal was bled to death from the carotid artery, and the lungs were examined in order to determine the distribution of the fluid.

RESULTS

Horizontal and Head Up Positions.—In these two positions (11 cats horizontal, 1 head up), the fluid injected into the tracheal cannula disappeared at once. At necropsy, the methylene blue-stained fluid was found distributed throughout the portions of both lungs which were most dependent at the time of the injection.

Head Down Position.—In this position (2 cats head down at an angle of 15 degrees with horizontal), although the fluid entered the cannula with each inspira-

tion, all of it was ejected by the succeeding expiration created by the elastic recoil of the chest wall. At necropsy, the lungs of these animals contained no methylene blue stain.

DISCUSSION

The conditions of the experiment, except for differences in posture, were identical for all animals. They were arranged to imitate conditions found frequently in infants asphyxiated at birth, with respect to: (1) Size of subject; (2) degree of respiratory paralysis; (3) frequency and depth of artificially induced respiration when an asphyxiated infant is undergoing similar treatment; and (4) the consistency of the fluid mixture found in the trachea of the newborn.

The weights of the cats, about 6 pounds, were approximately those of newborn infants. The respiratory paralysis produced by the curare was complete, as is seen often in the asphyxia of the newborn. The respirator was regulated so that the rate and depth of artificial respiration were equivalent to those which had been found adequate for maintaining satisfactory aeration in a large series of paralyzed cats, and as employed clinically in the treatment of asphyxiated infants. The injected fluid was similar in consistency to that found in the respiratory tract of newborn infants. It was slightly viscous, yet flowed readily.

The significant observation resulting from these experiments is "that the subatmospheric pressure applied to the chest, which was sufficient to maintain life, was incapable of raising fluid in the trachea against the force of gravity." On the basis of this observation, it appears that posture plays an important rôle in the movement of fluid which is present in the trachea of the newborn infant. It would seem advisable, therefore, to utilize the force of gravity at the time of birth as a prophylaxis against the inhalation of fluid. For this purpose, a position of the body at an angle of at least 15 degrees with the horizontal, head down, would be indicated.

REFERENCE

(1) *Murphy, D. P., Drinker, C. K., and Drinker, P.:* Arch. Int. Med. 47: 424, 1931.

TWO CASES OF CONGENITAL HEART DISEASE IN WHICH THE DIAGNOSIS WAS MADE BEFORE BIRTH*

A. L. Dippel, M.D., Baltimore, Md.

(From the Department of Obstetrics, the Johns Hopkins University and Hospital)

THE following two cases would seem to be of particular interest because in each a diagnosis of a congenital anomaly of the fetal heart was made before delivery, in the one instance during pregnancy and in the other during labor.

Case 1.—Mrs. B. was a thirty-four-year-old, white secundigravida, who had been making regular visits to the Obstetrical Dispensary of Johns Hopkins Hospital since she was three and one-half months pregnant. Her family history was essentially negative. Her only serious illness had been scarlet fever at the age of seven years. Her first pregnancy was terminated seven years before by the spontaneous delivery of a normal full-term male child. Her general physical examination showed nothing abnormal and her pregnancy progressed without incident.

One week before the estimated date of confinement, the fetal heart presented a peculiar souffle-like sound, which was at first thought to be a funic souffle. Upon more careful auscultation, however, a definite irregularity was noted in the fetal heart tones. There were frequent extrasystoles and a long, loud systolic murmur was clearly audible over a wide area. Deep pressure with the stethoscope failed to affect either the duration or the intensity of this murmur. In view of these facts it was felt that we were dealing with a structural anomaly of the fetal heart and such a diagnosis was made, bearing in mind a patent interventricular septum as the probable lesion.

The patient went into labor spontaneously two days later, when it was observed that the irregularities of the fetal heart which had been noted at her last prenatal visit, were still present exactly as before. She was delivered of a male child weighing 2,650 gm. (5 pounds, 13¼ ounces) after an eighteen-hour labor. The child appeared to be a normal, full-term infant; he cried spontaneously and lustily, and gave no outward appearance of any gross abnormality. However, on auscultation, the changes in the heart sounds heard before delivery were now more clearly evident and better oriented. The long, loud systolic murmur was heard over the whole precordium with maximum intensity over the third left intercostal space, making a diagnosis of patent interventricular septum the most likely. Thirty-six hours later, however, the point of maximum intensity of the systolic murmur was found over the first left intercostal space, and it accordingly seemed probable that we were dealing also with a patent ductus arteriosus. Twelve hours after delivery cyanosis began to appear; this was general in extent, but only moderate in degree. It was then felt that a transposition of the great vessels might be present as that anomaly without any others could account for the persistent cyanosis. Valvular sounds were heard over the pulmonic area but these were shown at autopsy to have been aortic sounds. The baby did poorly, became more and more cyanotic, took very little nourishment, and lost rapidly in weight as the cyanosis deepened; edema of the extremities appeared and increased; the respirations became more irregular and labored, and the infant died at the end of sixty hours.

*Read before the Baltimore Obstetrical and Gynecological Society, January 13, 1933.

A complete autopsy was performed and the heart dissected by Dr. Frank B. Kindell. Aside from the heart findings and anasarca, there were no significant observations. The heart showed several anomalies: transposition of the great vessels,

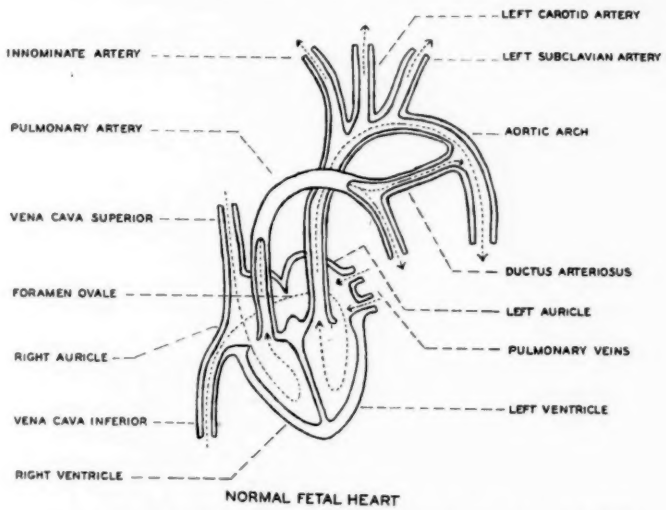


Fig. 1.—Showing the circulation in the normal fetal heart.

a large patent foramen ovale, a rudimentary tricuspid valve, a small patent interventricular septum, and small hemangiomas on the leaflets of the mitral valve. The left ventricle was rudimentary while the right ventricle was markedly hypertrophied and dilated. The ductus arteriosus was patent and almost as large as the aortic

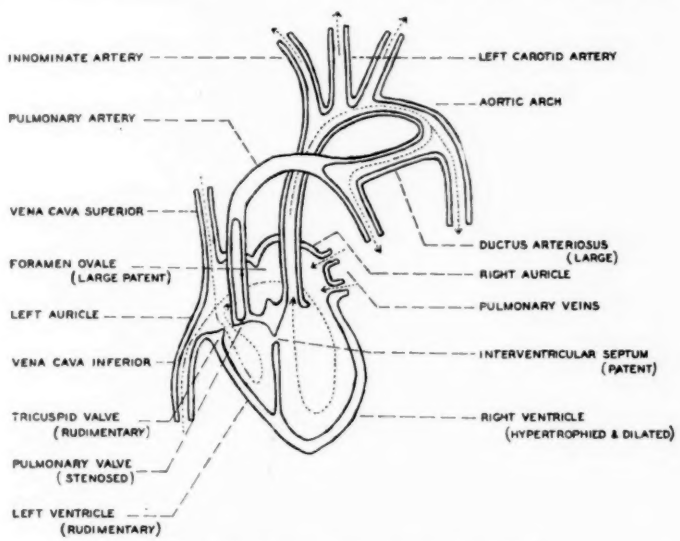


Fig. 2.—Showing the circulatory change present in the fetal heart described in Case 1.

arch. The conus arteriosus was absent and the pulmonary artery showed such a marked stenosis at its valve that no appreciable amount of blood could enter the pulmonary circulation in the usual way. In reconstructing this picture, we see that

venous blood entered the left auricle, and, due to the rudimentary left ventricle and stenosed pulmonary artery, passed through the large patent foramen ovale into the right auricle. Here it became mixed with oxygenated blood, passed on through the right ventricle into the aorta and systemic circulation and gained entry to the pulmonary artery and pulmonic circulation by flowing through the large ductus arteriosus in the direction opposite the normal fetal course. The defect in the interventricular septum was so small as to allow only a small amount of blood to pass from one ventricle to the other.

CASE 2.—Mrs. W. was a twenty-three-year-old, white secundigravida. Her family and medical history were not significant and her physical examination revealed nothing noteworthy save a generally contracted typical pelvis. The first child was a normal 3,835 gm. (8½ pound) male infant delivered after twenty-four hours of non-

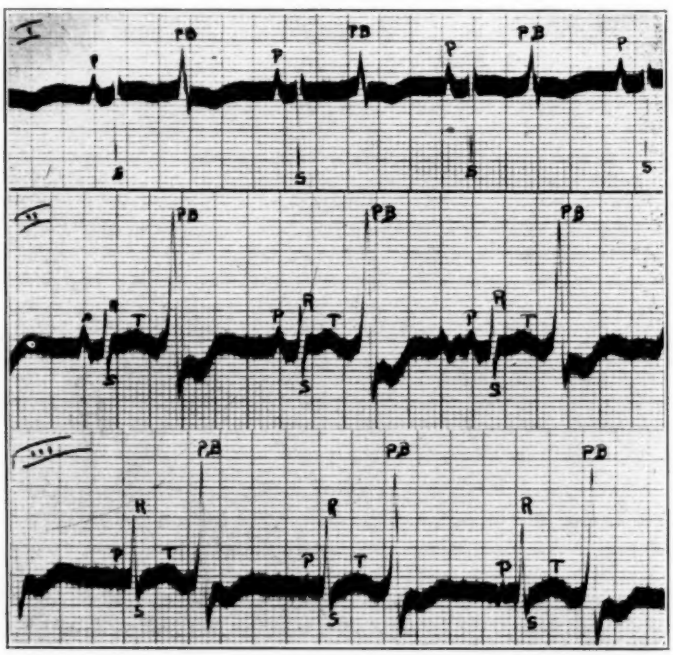


Fig. 3.—Showing the electrocardiogram of the fetal heart described in Case 2, the principal changes being bigeminal rhythm, dextrogram and ventricular extrasystoles.

progressive labor, by low cervical cesarean section with cephalopelvic disproportion as the indication. The second pregnancy was normal except for a slight disproportion noted during the last two antenatal weeks. She was admitted to the delivery floor at term and in early labor. At this time the surprising fact was discovered that the fetal heart rate was only 50 beats per minute. This same slow rate, moreover, persisted throughout labor. The rhythm, however, was regular. A careful examination failed to reveal any cause for the abnormally slow heart rate. A 3,025 gm. (6 pound, 10½ ounce), apparently normal, female child was delivered spontaneously after an eighteen-hour labor. Its color was good and it cried well immediately after delivery. Aside from its slow rate, the fetal heart showed nothing abnormal except an occasional extrasystole. An electrocardiogram was taken and the diagnosis given as: normal sinus rhythm, bigeminal rhythm, dextrogram, rate 67, and frequent ventricular extrasystoles. At the end of the second day, the first of a few

cyanotic attacks appeared with dyspnea, increased heart rate, and general collapse. Death occurred at the end of eighty-seven hours during the most severe cyanotic and dyspneic attack.

The autopsy by Dr. Kindell showed a stenosis of the isthmus of the aorta, patent foramen ovale, defect in the interventricular septum, patent ductus arteriosus, and extensive central liver necrosis with chronic passive congestion of the liver, and hemorrhages in the lungs.

Here, then, we have two cases of congenital heart disease in which the diagnosis was made during pregnancy and labor and confirmed clinically at birth and pathologically at autopsy. Fetal heart sounds and their irregularities have been observed and studied for more than a century. For the most part, however, investigators have concerned themselves with variations in the rate of the fetal heart, only a few having studied the character of the sounds themselves. The great majority of cases reported have been those of true sinus arhythmia. These are not infrequently encountered in the prenatal clinic and are characterized by the fact that they disappear either immediately or within ten to fifteen days after delivery. Such sinus arhythmias are of little or no clinical significance and are probably best explained on the basis of a myogenic or neurogenic origin, the young heart having a relatively unstable pacemaker.

The cases of actual cardiac disease of the fetus suspected or diagnosed during pregnancy are few in number. Apparently the first case was that reported by Massman[1] of Berlin, who in 1854 observed an unusual murmur in the fetal heart sounds, correlated it with a congenital heart lesion, and confirmed his suspicion at autopsy. In 1880, Barth[2] in Paris, heard a harsh murmur replacing the first fetal heart tone, thought it suggestive of an organic lesion, and at autopsy of the stillborn child confirmed his diagnosis of a congenital heart lesion. In this country, Padgett[3] of Nashville, in 1894, detected a harsh systolic murmur during auscultation of the fetal heart in pregnancy; he made the diagnosis of mitral heart disease of the unborn infant, and confirmed his diagnosis during examination of the infant after birth. Bellot,[4] 1895, and Andry and Lacroix,[5] 1890, made similar observations.

In 1926, Sampson, McCalla, and Kerr,[6] working on phonocardiography of the human fetus reported 31 cases of fetal cardiac irregularities, but in only one instance was there a congenital heart lesion. Hyman[7] of New York in 1930, doing similar work, obtained a fetal phonocardiogram in one of his 21 cases, which was similar to the electrocardiograms seen in adult cases of auricular fibrillation or flutter, but which was easily differentiated from his other cases of fetal sinus arhythmia.

In conclusion, cases such as we have reported serve to show that murmurs of the fetal heart, irregularities of rhythm and pronounced slowing of the rate, may in occasional instances be due to congenital heart disease, a diagnosis which can be made before delivery if careful attention is given to the character of the heart sounds.

REFERENCES

(1) *Massman:* Monatschr. f. Geburtsh. u. Frauenkran. **4**: 81, 1854. (2) *Barth, H.:* Quoted by J. W. Ballantyne, Manual of Antenatal Pathology, William Wood and Co. **2**: 509, 1904. (3) *Padgett, H.:* South. Practitioner **16**: 318, 1894. (4) *Bellot:* Quoted by J. W. Ballantyne, Manual of Antenatal Pathology, William Wood and Co. **1**: 372, 1902. (5) *Andry, C., and Lacroix, E.:* Quoted by J. W. Ballantyne, Manual of Antenatal Pathology, William Wood and Co. **2**: 509, 1904. (6) *Sampson, J. J., McCalla, R. S., and Kerr, Wm. J.:* Am. Heart J. **1**: 717, 1926. (7) *Hyman, A. S.:* Am. J. Obst. & Gynec. **20**: 332, 1930.

American Journal of Obstetrics and Gynecology

GEORGE W. KOSMAK, M.D., EDITOR HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

Editorial Comment

ANOTHER STUDY OF PUERPERAL MORTALITY

MUCH has been said and written about the deaths associated with childbearing in the United States as well as in foreign countries. This nation, in particular, has been accused of "paying less attention to the lives of its prospective mothers than to its cattle." Such statements seem exaggerated and must be accepted for what they are worth. There is no doubt, however, that obstetric art has not kept pace with the great advances in obstetric science during the last century. Why there should be a discrepancy has not been satisfactorily determined, but apparently there are certain underlying factors plainly evident in the conclusions reached in the records of those who have given careful thought to the matter.

Mortality rates in general, with a few notable exceptions, have been reduced within the last quarter of a century, while the deaths associated with childbearing are practically unchanged in number. It seems difficult to account for this apparent anomaly, but competent observers all point to causes that essentially are remedial. The studies of Adair and of Plass, with their coworkers, as well as the recently published report from the Federal Children's Bureau, leave one with an uncomfortable feeling that the indicated shortcomings in obstetric practice have not been met satisfactorily by the medical profession. An addition to these studies is a noteworthy report made by the special committee of the New York Academy of Medicine which undertook to investigate, during a three-year period, each puerperal death in New York City within a week or two of its occurrence, while the related facts were still fresh in the minds of the attendants. This document deserves thoughtful consideration for it has been carefully put together and most of its conclusions are in accord with those from other sources.

As a basis for the study, reference to numbers will be necessary. The Greater City of New York has a population of approximately 7,000,000 and the birth rate has declined steadily from 23.4 per thousand in 1920 to about 15.2 in 1932. The actual live births totaled 346,863 for 1930, 1931, and 1932. The general death rate during this period varied from 12.9 to 10.3. The infant mortality per 1,000 live births was reduced from 85.4 to 50.9. The total maternal mortality varied but little, 5.33 in 1920; 5.69 in 1932. Puerperal septicemia, excluding that after cesarean section, was 1.31 in 1920, 1.54 in 1932, with slight drops below these figures during the intervening years. About 70 per cent of all the births took place in hospitals; a steady increase during the past two decades is noteworthy, although apparently improved facilities for confinement showed no corresponding effect on the puerperal death rate.

The attendants in all the fatal cases were classified according to their type of practice. The majority, as might be expected, were attended by "obstetricians" (68.4 per cent), but a fact of great interest developed when a group denominated "other specialists" was analyzed. This excluded general practitioners, surgeons, and midwives. A recital of the make-up of this group is of moment: pediatricians attended 20 fatal cases, otolaryngolosists 11, orthopedists 5, urologists 3, ophthalmologists 3, radiologists 3, anesthetists and dermatologists, each one, or a total of 47. The deliveries in these cases were operative, including many cesarean sections. It is perhaps unnecessary to discuss the matter further; conclusions are self-evident.

A careful analysis of the fatalities which form the basis of the report discloses certain outstanding factors which force themselves on one's attention; namely, lack of proper antenatal care, meddlesome, too frequent and incompetent operative interference. These, with a few others, point clearly to the conclusion that the question of preventability in obstetric practice has not been sufficiently stressed. Hemorrhage, shock, and sepsis can be avoided or overcome; they are less likely to occur in natural deliveries than with untimely or unskilled interference. Again, when we find that deaths following cesarean section constituted almost 20 per cent of the total number, it would be fair to assume that this operation is more difficult and dangerous than is usually admitted.

Taking into consideration the associated factors, the committee was forced to the conclusion that approximately 65 per cent of the deaths in this community were preventable, either on the part of the attendant or the patient. Errors in diagnosis, general incompetence, carelessness and a tendency to underestimate the seriousness of obstetric operations, stand out in the judgment passed on the physician. Here also must be included unsupervised activities of insufficiently trained hospital internes and junior members of attending staffs. The pa-

tient's responsibility resided largely in her failure to secure suitable care even when this was available or in a lack of cooperation with the physician. The midwife was held responsible in a comparatively small number of cases; incompetence, carelessness, ignorance and lack of supervision appear to constitute her faults, conditions readily possible of control and improvement.

The various sections of the report cannot be reviewed in detail here, but their reading will make it quite evident that so far as New York City is concerned, this document constitutes an indictment of, as well as a challenge to, the medical profession, which it must answer. The conclusions and recommendations proposed by the committee should be made a matter of careful study not only by the members of special societies interested in obstetrics, but by the general practitioner as well, and the public must likewise be informed of its interests and obligations in the matter. It is only by a concerted effort that improvement will come about: medical students and internes must be more thoroughly instructed in obstetrics, proprietary hospitals and sanitaria must be carefully scrutinized by proper public authorities, the situation as regards midwife practice must be altered, greater respect toward operative procedures must be developed in the mind of the practitioner. The ease with which the latter may be conducted, particularly in the unsupervised smaller hospitals and nursing homes, leads to their frequent abuse and to fatal results.

This latest report on maternal mortality is not pleasant reading; it will arouse resentment, perhaps indignation, but its facts are amply proved. It is a courageous document, fearlessly presented, and should stimulate similar investigations elsewhere, for, when a community begins to assess its own facilities so far as securing safety for prospective mothers is concerned, measures will be taken to correct whatever faults may be found. And in this process the medical profession must take a leading part, for this as well as other investigations leaves an impression that the hazards of childbearing are greater than they need be and that the responsibility for reducing them in any given community depends largely on its physicians. It is to be hoped that they will accept the challenge.

Society Transactions

OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF MAY 4, 1933

The following papers presented:

Contraception. A Neglected Field for Preventive Medicine. Dr. Owen J. Toland. (See page 52.)

Nembutal and Scopolamine Analgesia in Childbirth With a Report of 160 Cases. Dr. L. Averett. (See page 109.)

Trials and Triumphs of Medicine. Dr. Charles S. Barnes. Presidential address.

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF MAY 19, 1933

The following papers were presented:

A Modification in the Technic of the Bell-Beuttner Operation. Dr. F. H. Falls. (See page 89.)

A Consideration of Chronic Cervicitis and of Its Operative Treatment. Dr. E. A. Bullard.

Failures in Tubal Sterilization (Madlener). Dr. W. H. Rubovits and Dr. A. J. Kobak. (See page 12.)

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF JUNE 16, 1933

The following papers were presented:

Theca Cell Tumors of the Ovary. Dr. P. J. Melnick and Dr. A. E. Kanter. (See page 41.)

The Significance of Menstrual Disturbances in Pulmonary Tuberculosis. Dr. H. C. Hesseltine and Dr. W. M. Spear. (See page 32.)

Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

THE MATERNAL MORTALITY IN 34,900 DELIVERIES TOGETHER WITH AN ANALYSIS OF 92 DEATHS*

SAMUEL J. SCADRON, M.D., F.A.C.S., NEW YORK CITY

(From the Service of the Jewish Maternity Hospital)

FOR the past decade, the subject of maternal mortality has enlisted the interest of both the lay and medical public. The comparative studies compiled in this and other countries and the increase in publicity given our inordinately high obstetric death rate, has centered the attention and discussion of many groups upon this problem.

Inasmuch as we have unquestionably made material strides in the advance of our knowledge of ante- and postpartum care, and have improved to no inconsiderable extent, our obstetric and surgical technic, it is but reasonable to expect that a consistently lower maternal death rate will result. Unfortunately, we find little or no improvement.

Before it is possible to present preventative measures for reducing the mortality associated with childbearing, we must analyze its causes. Since we have all too few systematic reports of obstetric fatalities, I desire to present these statistics of 34,900 consecutive deliveries at the Jewish Maternity Hospital of New York City, in order to demonstrate the results of a carefully supervised hospital service.

In this series, we report 92 maternal deaths, which is a rate of 2.6 per thousand. (In the registration areas of the United States, the death rate for 1929 was 7 per thousand.) These 92 deaths occurred in the hospital, with the exception of two patients who were brought in in a moribund condition after a difficult home delivery. The greatest number of deaths for any one year was seven; and during two years, there were no fatalities. Thirty-three fatalities occurred in primiparas, 13 deaths in para two and three, 12 deaths in para four, 4 deaths in para five and six, 5 deaths in para seven and eight, 2 in para nine, and 1 death in a multipara twelve. Over one-third of the deaths occurred in primiparas, while about 23 per cent of the mortality rate occurred in paras three, four, and five. The remainder of the deaths are in multiparas after the fifth delivery.

If we divide the period over which these patients were delivered into intervals of twelve years each, we find that during the years from 1909 to 1920, we delivered 16,329 patients with 47 deaths (a rate of 2.7 per thousand); while during the years from 1920 to 1932, there were 18,571 deliveries with 45 deaths (a rate of 2.6 per thousand). Thus it may be observed that in the past twelve years, we show but slight improvement in our total number of deaths.

*Presented at a meeting of the Medical Society of the County of New York, Nov. 28, 1932.

The grouping of cases in accordance with the cause of death may be summarized as follows:

Sepsis	36 cases,	39.1%	or 1 in	970	deliveries.
Hemorrhage	13 cases,	14.1%	or 1 in	1,915	deliveries.
Eclampsia	11 cases,	11.9%	or 1 in	3,173	deliveries.
Ruptured Uterus	9 cases,	9.6%	or 1 in	3,865	deliveries.
Cardiac	7 cases,	7.6%	or 1 in	4,985	deliveries.
Pneumonia	4 cases,	4.2%	or 1 in	8,725	deliveries.
Shock	3 cases,	3.2%	or 1 in	11,634	deliveries.
Toxemia	2 cases,	2.1%	or 1 in	17,450	deliveries.
Intestinal Obstruction	2 cases,	2.1%	or 1 in	17,450	deliveries.
Embolism	2 cases,	2.1%	or 1 in	17,450	deliveries.
Nephritis	2 cases,	2.1%	or 1 in	17,450	deliveries
Meningitis	1 case,	1.0%	or 1 in	34,900	deliveries

Thus, we may conclude that about 75 per cent of the death rate (69 cases) was due to more or less preventable causes, i.e., infection, hemorrhage, toxemia, and ruptured uterus.

The methods of delivery and operative procedures were as follows:

Spontaneous delivery	in 26 cases,	28%
Forceps delivery	in 15 cases,	16.3%
Version delivery	in 17 cases,	18.4%
Vaginal cesarean	in 1 case,	1.08%
Abdominal cesarean	in 17 cases,	18.4%
Porro cesarean	in 1 case,	1.08%
Undelivered	in 7 cases,	7.6%
Craniotomy	in 4 cases,	4.3%
Breech delivery	in 4 cases,	4.3%

It is of interest to note that in the absence of interference during delivery, there were 8 cases attributable to sepsis: 2 of these patients died from hemorrhage in placenta previa, 3 from eclampsia, 3 from cardiac complications, and 3 from ruptured uterus, nearly all of which are preventable causes. Cesarean section was accountable for death in 17 patients, 11 of whom died from sepsis, 3 from hemorrhage in placenta previa, 1 from pneumonia, and 2 from intestinal obstruction, 1 case of which occurred in the antepartum period. Version was performed in 17 cases which ended fatally: 3 of the deaths were from sepsis, 6 from placenta previa, 5 from ruptured uterus, 1 from eclampsia, 1 from cardiac complications, and 1 patient died of anesthesia shock.

Forceps delivery in 15 cases resulted in 6 deaths from sepsis following prolonged labor, 3 from eclampsia, and in the death of 2 cardiac patients with decompensated hearts. Embolism, toxemia, shock, and pneumonia were the direct cause of death after the application of forceps.

Undelivered cases resulted in 7 deaths, all of which were not preventable. One patient was brought in with placenta previa; 1 entered the hospital almost exsanguinated; 4 patients died with eclampsia, 1 almost before we had opportunity to render treatment; and 1 patient, a cardiac case, was brought in with decompensated heart, dying shortly after admission.

Craniotomy was responsible for 4 deaths, the result of sepsis and shock. Porro cesarean was accountable for 1 death from postoperative hemorrhage.

Considering the causes of death in relation to the parities, it is of interest to note that there is a greater risk in primiparas; and this risk diminishes up to the fourth labor when there is an increased risk with successive pregnancies. As far as

occurrence of controllable causes is concerned, we find that puerperal sepsis was responsible for 14 out of 33 primipara deaths, a rate of 42.4 per cent; and this rate decreased in multiparas. Eclampsia accounted for 8 of the 33 primipara deaths (25 per cent); the remaining 3 cases were in paras two, three, and four. Postpartum hemorrhage was the cause equally of 4 deaths in para one and para three. We have not a single case of a ruptured uterus in a primipara, although there is a record of a death each in a multipara two, three, and seven from this cause, and 2 deaths each in paras four, six, and eight. Shock occurred once each in paras four, seven, and eight.

A tabulation of the method of delivery in relation to the parities shows that the greatest number of deaths in the spontaneous births occurred in primiparas, while the incidence of death was about equally divided among the remaining paras. However, the incidence of death was increased proportionately with each succeeding pregnancy. Forceps operation was performed in 9 out of 15 fatalities in primiparas, and version in 6 out of 17 deaths in primiparas. Abdominal cesarean section was performed 5 times in both para one and para two, 3 times in both para three and para four, and once in a para seven. Of the deaths in undelivered cases, 3 were primiparas, 2 were multipara two, 1 was a para three, and 1 a para six.

In discussing the controllable causes, we find that puerperal sepsis was the cause of the greatest number of deaths. Of the 36 fatalities from this cause, 8 occurred in spontaneous births, 11 after abdominal cesarean sections (5 following placenta previa), 3 deaths followed craniotomies, 1 occurred in an undelivered patient, 6 were from forceps deliveries, 1 followed a vaginal cesarean section, and there was 1 death from antepartum sepsis.

In this series of 36 deaths from sepsis, the rate is 39.1 per cent, which compares favorably with the rates reported in other large cities of this country. (Philadelphia, 37.8 per cent; Chicago, 41.5 per cent; Detroit, 49.3 per cent; and Los Angeles, 51.6 per cent.) Ronsheim reports from the Jewish Hospital of Brooklyn a rate of 40 per cent for 1930. In New York City during 1930, we have the figures of 122,811 deliveries with 667 puerperal deaths, 113 of which were charged to sepsis. In 1931, in New York City, 115,621 deliveries were reported, with a mortality of 6.1 per thousand; and puerperal sepsis was given as the cause of 187 deaths.

Whenever an underlying sepsis was the actual cause of death in any of our series, we disregarded a terminal pneumonia or eclampsia, and classified the case definitely as sepsis, as stated by the death certificate.

The direct inoculation of bacteria into the wounds before or after delivery cannot be regarded as the sole cause of sepsis. In our series of 36 septic deaths, 8 patients died after spontaneous delivery.

Prolonged labor, instrumentation, hemorrhage, and prolonged deep anesthesia are predisposing factors in the causation of sepsis. Forceps, version, craniotomy, and difficult breech extractions were accountable for 15 of the 36 septic fatalities. Therefore, our conclusion is that early interference without definite indications is a factor in the high maternal mortality rate.

Until recently, vaginal examination under strict asepsis was routinely performed. For the past six years, however, we have employed rectal examination only, on admission and during labor. Vaginal examinations were done solely when the interne or attending obstetrician was unable to determine definitely the position and presentation by rectal or abdominal palpation. We did not, however, find that this procedure lowered the morbidity or mortality rates. We believe, therefore, that the sole disadvantage in the vaginal routine is unnecessary manipulation of the cervix in an effort to determine the exact position of the presenting part; and we do not believe that this risk would present itself with a well-trained obstetrician.

For a short period, we made a rule on our service to avoid all vaginal and rectal examinations on admission or during labor. Position and presentation were determined so far as was possible by abdominal palpation. The progress of labor was judged by the character of the pains, the uterine contractions, and the natural expulsive efforts of the mother. We made some few exceptions, naturally, such as sudden rupture of membranes or bleeding. A series of about 150 cases managed in this fashion was compared with a series subjected to vaginal and rectal examinations; and since there was no appreciable advantage, we desisted because of the objections of the interne staff.

We have also made another interesting experiment in the problem of reducing maternal mortality. Since October, 1926, we have used mercurochrome in our delivery and labor rooms. This represents a trial period of six years, and I have made the following comparative table of results:

1909 to 1914:	6,254 deliveries:	10 septic deaths;	1 in 625
1915 to 1920:	10,065 deliveries:	13 septic deaths;	1 in 774
1921 to 1926:	10,785 deliveries:	10 septic deaths;	1 in 1,078
1927 to 1932:	7,996 deliveries:	3 septic deaths;	1 in 2,665

We have therefore felt that the slight improvement in our septic death rate might be attributable to our change in the vaginal antiseptic used; and we have continued to use mercurochrome, and to check up on our results.

In our records of 34,900 deliveries, we report 215 abdominal cesareans with 11 deaths. Of these fatalities, 2 patients were operated upon for placenta previa, 2 for eclampsia, and 7 for contracted pelvis. None of the 11 deaths occurred prior to the introduction of laparotrachelotomy and transperitoneal cesarean.

In the first fourteen years, that is, the interval between 1909 and 1923, we performed 152 cesarean sections out of 22,146 deliveries, an incidence of 1 out of 145 cases. In the second interval, 1923 to date, we have performed 51 cesareans out of 12,754 deliveries, an incidence of 1 in 250 cases. This startling decrease in the incidence of cesarean sections is due in part to our present-day command of other operative procedures than the classical operation. Thus, our patients are first permitted a true test of labor, with the result that they deliver normally in many cases.

Hemorrhage was responsible for 13 deaths, a rate of 14.5 per cent. Twelve of these fatalities were due to placenta previa and 1 followed a Porro cesarean. It would appear that death from this controllable cause would indicate improper management. It is certain that if we could institute treatment in a sufficiently early stage of hemorrhage, we could expect a decrease in mortality.

We have recently published an analysis of 158 cases of placenta previa from our service, in which Dr. Leo Moskowitz reports 12 deaths—a rate of 5 per cent. Since the publication of this series, we have had 9 more cases: 3 central, 1 partial, and 5 marginal placenta previa, with no resulting deaths. Of the 12 deaths reported by Dr. Moskowitz, 4 occurred in marginal placenta previa, 2 in partial, and 6 in central placenta previas. Death occurred following these procedures: 2 after insertion of bag and spontaneous delivery; 1 after Braxton-Hicks bipolar version; 1 undelivered following insertion of bag (shock and hemorrhage); 2 after bagging and version; 3 after internal version; and 3 after a classical cesarean section. From 1909 to 1925, we report 11 deaths out of 133 cases; and in the second interval from 1925 to 1932, only 1 death out of 34 cases. This patient had a hemorrhage for two days in the home. A cesarean section was performed with a spinal anesthesia, and she died two hours postoperative from shock. Nine patients from the first series of 11 deaths did not receive transfusions; and we credit our recent low mortality rate in placenta previa cases to timely blood transfusions and efficacious packing.

We therefore believe that in order to reduce maternal mortality from this cause, we must deal promptly with all cases after the first hemorrhage. In our series, we have been particularly successful with routine insertion of a bag extraovularly in marginal and partial placenta previas. In central cases, at or near term, with viable child, abdominal cesarean section is our choice of procedure. In all types, we advocate iodoform gauze packing after the expulsion or removal of the placenta, as we believe that this prevents uterine relaxation and aids in the prevention of blood loss. Blood transfusion should be done in all cases at once, before and after delivery, if there is a systolic pressure of one hundred or below. We are convinced that many of our earlier cases might have been saved by this method.

Eclampsia accounted for 11 deaths in our series of 105 reported eclamptic and 68 preeclamptic cases. From our first series (1909 to 1918) we had 49 cases out of 12,519 deliveries, an incidence of 1 in 255 cases; in our second series (1918 to 1932) we show 46 eclamptics out of 22,381 deliveries, an incidence of 1 in 486 cases. This decrease since 1918 is directly due to a careful system of check-up in our prenatal clinic by social service nurses, who use every means of persuasion to gain prompt regular attendance on the part of the antepartum patients. Thus, we closely observe all instances of rising pressure, edema, and disturbed kidney function. Our management of these cases is, in the main, conservative. In the early days, when cesarean section was advocated in primiparas with long rigid cervices, at term, we performed three sections for eclampsia; two of the patients died of sepsis. This practice is still followed by some. We, however, do not temporize; we believe in inducing labor immediately after convulsions, and then following with the usual medical treatment, i.e., magnesium sulphate, morphine, glucose, etc. We do not resort to accouchement forcé or any method of rapid dilatation of the cervix.

Our preeclamptic patients are hospitalized; and if we obtain no response to routine medical treatment, we never temporize, but advise immediate induction of labor. We had one sudden fatality in our preeclamptics while the patient was apparently improving under medical care. Of the remaining 8 cases, 2 patients were brought into the hospital moribund, and died soon after admission.

Ruptured uterus was responsible for 9 deaths in 13 cases. Of these 9 fatalities, 3 were spontaneous, 5 occurred after version, and 1 after breech extraction had been performed. It is of interest that we have no cases of rupture in primiparous mothers, only one case in a para three, and two ruptures each in paras four, six, and eight, while one case of rupture in a para seven is reported. In the group of 3 spontaneous ruptures, we find one due to the administration of 1 c.c. of pituitrin to a para seven patient, who had a cervical dystocia and a marked pendulous abdomen. (I must state, however, that this occurred in 1912, when this drug was first introduced.) Another of the three spontaneous cases reported was in a patient who had a history of an incomplete rupture one and one-half years previously, and who had been advised to have an elective cesarean on this occasion. She disregarded the advice, entered the hospital well-advanced in labor, suffered a uterine rupture, and died undelivered, awaiting preoperative preparation. The third case reported was a spontaneous uterine rupture through the previous cesarean incision.

With our added age and experience we have learned to regard multiparas subject to dystocia with the utmost respect. There is a *locus minoris resistentiae* in every multigravid uterus, due undoubtedly in many cases, to previous manipulation or instrumentation resulting in cicatrized areas. In these cases, and in patients with pendulous abdomens, engagement of the presenting part is usually interfered with or delayed, a fact which often leads to premature interference.

Cardiac deaths must of necessity be considered inevitable. Of the 7 reported in our series, 2 were sudden fatalities from myocarditis and angina pectoris in

paras eight and five, respectively, following delivery. One patient was admitted with decompensation and pulmonary edema, and died soon after admission.

To evaluate an obstetric death in comparison with a surgical or medical fatality, it is obvious that the obstetric death is a greater shock to both family and accoucheur. Motherhood contracts with Nature for a normal physiologic labor and puerperium; but oftentimes Nature is most unkind, and it is then that science must intervene. In the final analysis, even the most scientific and impressive statistics bring no comfort to a family that has suffered a single maternal tragedy. If, however, we can, by consistent and conscientious research and statistics, aid in reducing these maternal fatalities by even a small percentage, we shall not feel these studies to have been in vain. It is by constant comparison and concentration of our methods and results that we shall benefit ourselves scientifically, improve our obstetric training and judgment, and eventually tend to reduce our maternal mortality rates.

In conclusion, we believe that our comparative decrease in our mortality rate in these 34,900 deliveries to be due to:

1. Increased efficiency in prenatal care, early recognition of toxemias, hospitalization of preeclamptics, interference in cases showing nonimprovement under medical care, conservative treatment of eclampsias, and termination of labor with the minimal amount of operative interference.

2. Prompt treatment of uterine bleeding, early cesarean section in central placenta previas, and prompt transfusion in all hemorrhage cases.

3. Careful choice in selection of cases for cesarean section, particularly in borderline cases, and utilization of methods other than the classical cesarean in potentially infected cases, i.e., the low flap, the transperitoneal, and the extraperitoneal of Latzko.

4. Greater respect for multiparas, particularly those with a previous history of difficult labor or instrumental delivery, and the avoidance of early operative interference.

993 Park Avenue.

Rodecurt, M.: Trichomonas Vaginalis, Ztschr. f. Geburtsh. u. Gynäk. **102:** 151, 1933.

A questionnaire concerning the significance and treatment of Trichomonas vaginalis was sent to all 907 members of the German Gynecological Society. Of 143 answering, 33 admitted having had no experience with this parasite. Opinion differed as to its being pathogenic or not. Rodecurt regards them as pathogenic. Various treatments were tried by the writer, who finally concluded that Yatren 105 (containing iodine), used successfully in the tropics against Trichomonas intestinalis, gives the most satisfactory results. Vaginal insertion of one suppository twice daily led to rapid improvement, later on one pill was used daily, finally one every three or four days. Treatment must be carried on for several weeks without interruption and even intensified during menstruation (2 pills at night).

Grover Liese.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

Collective Review

THE DIAGNOSIS AND TREATMENT OF SYPHILIS COMPLICATING PREGNANCY

NORMAN R. INGRAHAM, JR., M.D., AND JAMES E. KAHLER, M.D.,
PHILADELPHIA, PA.

(From the Department of Obstetrics, School of Medicine, University of Pennsylvania)

THE diagnosis of syphilis often under the most favorable circumstances a problem fraught with difficulties, becomes manifoldly harder when we are dealing with the disease in pregnant women, for here we have to do, in the vast majority of cases, with the almost symptomless and none too well understood period of latency. Perhaps more than 70 per cent of the women in whom the disease is found[40, 109] will profess total ignorance, not only of the source of the infection or the time of its inoculation, but even of any abnormality in themselves which they might attribute to the presence of a serious malady, so benign has the course of the spirochetal invasion in them been and so poor are their memories and powers of observation. To make matters more complicated, there will be found in any series of cases a number of women who have given birth to syphilitic children in the presence of a negative serological examination (cf. Stokes,[213] p. 999). This is particularly the case when the disease is of long standing, more especially when some, though not completely effective treatment has been instituted in the past. All these factors compel the physician who would detect the majority of syphilitic women in time to prevent an unfortunate termination of their pregnancy, to avail himself of all the diagnostic acumen and subsidiary aids he may possess. Contrary to some of the older opinions, the demonstration of syphilis in the infected child at the time of birth when treatment would be of the greatest benefit is often next to impossible. The value of antiluetic therapy in combating congenital syphilis, on the other hand, has been known for more than two hundred and fifty years[227] and has never been demonstrated more conclusively than in the last decade.

Though exact information on the subject is difficult to obtain, syphilis is a rather common disease. Its incidence among pregnant women will vary with the racial characteristics of the patients, with their social status and intelligence, with their age, but it is surprising to note that if statistics are taken from obstetric clinics throughout the civilized world, the general incidence will usually fall between 5 and 10 per cent (see Table I). Among the negro women, the occurrence of the disease is exceptionally high; ordinarily 15 per cent or more are infected.[101, 210, 234, 240] Jeans and Cooke[111] in their careful study of the distribution of syphilis among the pregnant women of St. Louis found that 5.7 per cent of the women of the poorer class harbored the disease as compared with about a 1 per cent incidence in the higher classes. The social distinction is, likewise, well exemplified in Philadelphia,

where, in 1931, the Child Health Society found the incidence in clinic patients to be about 5 per cent, while Toland[218] found a 7 per cent incidence at the Pennsylvania Hospital, and Schumann and Barnes[198] reported several years previously that more than 25 per cent pregnant women at the Philadelphia General Hospital gave posi-

TABLE I

THE INCIDENCE OF SYPHILIS IN PREGNANCY AS SHOWN BY VARIOUS AUTHORS (CF. SOLOMON[204])

AUTHOR		LOCALITY	PER CENT SYPHILITICS		NO. CASES IN SERIES
Bartholomew[14]	1924	Atlanta, Ga.	34		colored
Williams[240]	1920	Baltimore, Md.	2.5	(white)	4000
			16.3	(colored)	
Hinton[103]	1923	Boston, Mass., Lying-In	5.0		7121
		Florence Critt. Home	5.6		264
		Lowell Corp. Hosp.	2.5		370
		New England Hosp.	1.5		2672
Stillians[210]	1928	Chicago, Ill.	6.0	(white)	6954
			19.2	(colored)	814
Welz and VanNest[234]	1922	Detroit, Mich.	5.7	(white)	1467
			19.3	(colored)	
Bessesen[24]	1929	Minneapolis, Minn.	2.0		400
Commiskey[49]	1916	N. Y. C. Keys Co. Hosp.	8.0		1822
Goodman[91]	1920	N. Y. Sloan Mat. Hosp.	6.7		1320
Hemsath[101]	1931	N. Y. Lying-In Hosp.	2.5	(white)	6800
			12.0	(colored)	
Schumann and Barnes[198]	1921	Phila., Pa., General Hosp.	27.8		661
Toland[218]	1929	Phila., Pa., Penna. Hosp.	6.8		500
Report of Child Health Soc.	1931	Phila., Pa.	5.0		6885
Menten[155]	1918	Pittsburgh, Pa.	13.5		357
Jones[115]	1928	Providence, R. I.	1.3		1665
Stacy[209]	1932	St. Joseph, Mo.	8.4		
Jeans and Cooke[111]	1921	St. Louis, Mo.	3.0		2030
Sage[192]	1928	Univ. Neb. Coll. Med.	5.5		1200
Fowler[81]	1925	Univ. Oklahoma	1.2		265
Bacon[11]	1932		5.0		918
Parker[170]	1927		8.3		6300
Dodds[40, 62]	1927	Edinburgh Royal Mat.	6.5		2000
Cruickshank[54]	1922	Glasgow, Scotland	9.0		1900
Wells[233]	1929	Cape Town, S. Africa	28.2		1000
Boas and Gammeltoft[32]	1926	Copenhagen, Denmark	6.7		2200
Gammeltoft[85]	1928	Copenhagen, Denmark	5.5		22,383
Laurentier[131]	1931	Toulouse Hosp., France	5.2		957
	1926		11.1		
	1927		9.6		
	1928		6.0		
	1929		8.0		
	1930		5.0		
Richter[180]	1929	Berlin, Germany	16.0		6076
Spiegler[207]	1932	Frankfurt, Germany	5.1		7930
Wingen[243]	1919	Köln, Germany	6.5		
	1922		5.0		
	1930		2.0		
Morosoff and Raskin[162]	1930	Grauerman, Russia	6.0		14,869
Nakayama[165a]	1933	Tokyo, Japan	7.3		303

tive serology (cf. also Hinton[103] for class distinction in Boston hospitals). In this connection it is well to bear in mind that, as Belding[20] has shown, the disease is more prevalent in multiparas than in primiparas and that it is unwise to assume

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

Collective Review

THE DIAGNOSIS AND TREATMENT OF SYPHILIS COMPLICATING PREGNANCY

NORMAN R. INGRAHAM, JR., M.D., AND JAMES E. KAHLER, M.D.,
PHILADELPHIA, PA.

(From the Department of Obstetrics, School of Medicine, University of Pennsylvania)

THE diagnosis of syphilis often under the most favorable circumstances a problem fraught with difficulties, becomes manifoldly harder when we are dealing with the disease in pregnant women, for here we have to do, in the vast majority of cases, with the almost symptomless and none too well understood period of latency. Perhaps more than 70 per cent of the women in whom the disease is found[40, 109] will profess total ignorance, not only of the source of the infection or the time of its inoculation, but even of any abnormality in themselves which they might attribute to the presence of a serious malady, so benign has the course of the spirochetal invasion in them been and so poor are their memories and powers of observation. To make matters more complicated, there will be found in any series of cases a number of women who have given birth to syphilitic children in the presence of a negative serological examination (cf. Stokes,[213] p. 999). This is particularly the case when the disease is of long standing, more especially when some, though not completely effective treatment has been instituted in the past. All these factors compel the physician who would detect the majority of syphilitic women in time to prevent an unfortunate termination of their pregnancy, to avail himself of all the diagnostic acumen and subsidiary aids he may possess. Contrary to some of the older opinions, the demonstration of syphilis in the infected child at the time of birth when treatment would be of the greatest benefit is often next to impossible. The value of antiluetic therapy in combating congenital syphilis, on the other hand, has been known for more than two hundred and fifty years[227] and has never been demonstrated more conclusively than in the last decade.

Though exact information on the subject is difficult to obtain, syphilis is a rather common disease. Its incidence among pregnant women will vary with the racial characteristics of the patients, with their social status and intelligence, with their age, but it is surprising to note that if statistics are taken from obstetric clinics throughout the civilized world, the general incidence will usually fall between 5 and 10 per cent (see Table I). Among the negro women, the occurrence of the disease is exceptionally high; ordinarily 15 per cent or more are infected.[101, 210, 234, 240] Jeans and Cooke[111] in their careful study of the distribution of syphilis among the pregnant women of St. Louis found that 5.7 per cent of the women of the poorer class harbored the disease as compared with about a 1 per cent incidence in the higher classes. The social distinction is, likewise, well exemplified in Philadelphia,

where, in 1931, the Child Health Society found the incidence in clinic patients to be about 5 per cent, while Toland[218] found a 7 per cent incidence at the Pennsylvania Hospital, and Schumann and Barnes[198] reported several years previously that more than 25 per cent pregnant women at the Philadelphia General Hospital gave posi-

TABLE I

THE INCIDENCE OF SYPHILIS IN PREGNANCY AS SHOWN BY VARIOUS AUTHORS (CF. SOLOMON[204])

AUTHOR		LOCALITY	PER CENT SYPHILITICS		NO. CASES IN SERIES
Bartholomew[14]	1924	Atlanta, Ga.	34		colored
Williams[240]	1920	Baltimore, Md.	2.5	(white)	4000
			16.3	(colored)	
Hinton[103]	1923	Boston, Mass., Lying-In	5.0		7121
		Florence Critt. Home	5.6		264
		Lowell Corp. Hosp.	2.5		370
		New England Hosp.	1.5		2672
Stillians[210]	1928	Chicago, Ill.	6.0	(white)	6954
			19.2	(colored)	814
Welz and VanNest[234]	1922	Detroit, Mich.	5.7	(white)	1467
			19.3	(colored)	
Bessesen[24]	1929	Minneapolis, Minn.	2.0		400
Commiskey[49]	1916	N. Y. C. Keys Co. Hosp.	8.0		1822
Goodman[91]	1920	N. Y. Sloan Mat. Hosp.	6.7		1320
Hemsath[101]	1931	N. Y. Lying-In Hosp.	2.5	(white)	6800
			12.0	(colored)	
Schumann and Barnes[198]	1921	Phila., Pa., General Hosp.	27.8		661
Toland[218]	1929	Phila., Pa., Penna. Hosp.	6.8		500
Report of Child Health Soc.	1931	Phila., Pa.	5.0		6885
Menten[155]	1918	Pittsburgh, Pa.	13.5		357
Jones[115]	1928	Providence, R. I.	1.3		1665
Stacy[209]	1932	St. Joseph, Mo.	8.4		
Jeans and Cooke[111]	1921	St. Louis, Mo.	3.0		2030
Sage[192]	1928	Univ. Neb. Coll. Med.	5.5		1200
Fowler[81]	1925	Univ. Oklahoma	1.2		265
Bacon[11]	1932		5.0		918
Parker[170]	1927		8.3		6300
Dodds[40, 62]	1927	Edinburgh Royal Mat.	6.5		2000
Cruickshank[54]	1922	Glasgow, Scotland	9.0		1900
Wells[233]	1929	Cape Town, S. Africa	28.2		1000
Boas and Gammeltoft[32]	1926	Copenhagen, Denmark	6.7		2200
Gammeltoft[85]	1928	Copenhagen, Denmark	5.5		22,383
Laurentier[131]	1931	Toulouse Hosp., France	5.2		957
	1926		11.1		
	1927		9.6		
	1928		6.0		
	1929		8.0		
	1930		5.0		
Richter[180]	1929	Berlin, Germany	16.0		6076
Spiegler[207]	1932	Frankfurt, Germany	5.1		7930
Wingen[243]	1919	Köln, Germany	6.5		
	1922		5.0		
	1930		2.0		
Morosoff and Raskin[162]	1930	Grauerman, Russia	6.0		14,869
Nakayama[165a]	1933	Tokyo, Japan	7.3		303

tive serology (cf. also Hinton[103] for class distinction in Boston hospitals). In this connection it is well to bear in mind that, as Belding[20] has shown, the disease is more prevalent in multiparas than in primiparas and that it is unwise to assume

that because a woman was free from the disease at her first pregnancy, she still is so in her subsequent confinements.

To merely state that one in every ten or one in every twenty women in the childbearing age is a victim of this disease means little if its destructive influence on the products of conception and on the next generation, when syphilis is permitted to go untreated, are not fully realized. At present it is doubtful if any disease, even tuberculosis, is so destructive to child life and so disastrous to child health as syphilis.[4, 214, 244] To take only a few isolated statistics (Boas[29]), Kassowitz[116] found close to one-third of the fetuses died before birth; of those born alive 24 per cent succumbed in the first half year of life. In 239 pregnancies, likewise in syphilitic families, Fournier found that 176 of the fetuses died of syphilis, a mortality of 73 per cent. Perhaps no clearer study is to be found than that of Hochsinger,[105] published in 1910, in which he kept under observation 134 syphilitic

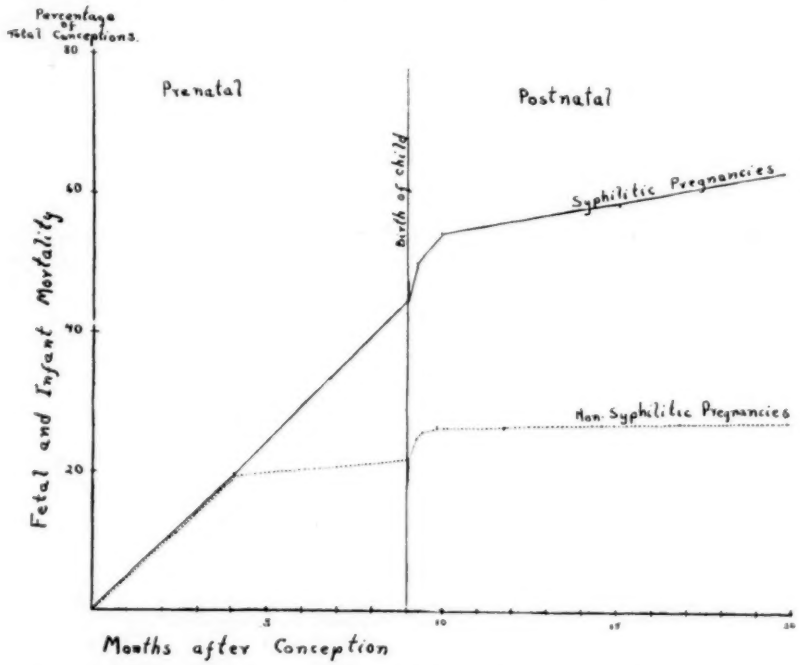


Chart 1.—Graphic representation of fetal and infant mortality resulting from untreated syphilitic pregnancies as compared with that in nonsyphilitic pregnancies.

Data from the following sources: Armstrong,[8] Bartholomew,[14] Belding,[20] Commiskey,[49] Corda,[51] Cruickshank[54, 55] Funkhouser and Dickson,[84] Gautier and Thevenod,[87] Hochsinger,[105] Jeans,[109] Klaften,[120] Lesne and Linossier-Ardoin,[137] McCord,[141, 146] Marshall,[152] Miles,[157] Moore,[160] Morosoff and Raskin,[162] Polak and Beres,[175] Pye-Smith,[177] Schwarz,[190] Whitehouse,[226] Williams,[238] Woodbury.[244]

families, some for as long as twenty-nine years and none for less than four years. In the 569 pregnancies which resulted, 253 (44.4 per cent) of the children were stillborn and 316 were born alive. Of these latter, 263 were syphilitic and only 53 were apparently healthy. Of the 263 syphilitics, 55 died before the fourth year. In this country, Williams, [239] in 1920, made the statement that in the case of white infants untreated syphilis exceeded all other causes of fetal death at Johns Hopkins except dystocia to which it ran a close second, while in the colored race it was the etiologic factor in 45.23 per cent cases. Seven years later McCord,[143] reporting from Atlanta, states, "In following the babies born of mothers with a positive Wassermann reaction, I have ascertained that 33 per cent of the women do not

leave the hospital with a live baby and that of those who do, 11 per cent lose their baby during the first few weeks of life; 25 per cent of the others develop a positive blood Wassermann reaction. The toll of syphilis in the colored race, at least in this part of the country, is unbelievable.'' Without dwelling further upon these individual reports, group studies will readily show that the incidence of stillbirths is easily eight times more frequent in the syphilitic individual than in the population at large and that, whereas the infant death rate in this disease during the first week of life is about three times that of the average for this country, by the end of the first year of life nearly four in every ten have perished, as compared with the generally accepted infant mortality rate of 80/1000 in the same period of time (Chart 1). Indeed, as might be supposed, a large number of the children who are alive are syphilitic. In the clinic class of patient a conservative estimate of the incidence of congenital syphilis would be about 5 per cent.[110, 111, 122, 204]

Pathogenesis of Syphilis in the Pregnant Woman.—Successful management of syphilis complicating pregnancy presupposes a knowledge of the pathogenesis of the disease in the parturient woman. Paracelsus' original concept of the infection being transferred by ''an unknown substance which mixes with the sperm and is transmitted to the new being'' (Bertaccini[21]), is considered today the least frequent mode of passage, if it occurs at all. For, though the semen is often infective[72, 127] even in the absence of other manifestations of the disease, the mother is most readily inoculated via the uterine cavity,[231] and possesses a positive Wassermann reaction or some other evidence of the disease in almost every case[32, 74, 207, 243] which is carefully studied, while the *Treponema pallidum* has never been demonstrated histologically in the fetus prior to the fourth month of pregnancy,[21, 85, 106] and it is usually not seen before the sixth month.[229] These arguments, of course, do not absolutely preclude this mode of transfer, especially in the light of the reasoning of Routh[188, 189, 190, 191] of the treponemicidal action of certain placental ferments, which has some measure of confirmation in the work of Manouilian,[150] and when one considers the experimental evidence of the existence of granular forms of the microorganism, but the fact remains that the mother is usually infected. It is in her we must detect the disease and through her we must treat her offspring.

While *Treponema pallidum* have been demonstrated in the ovum by Hoffmann and Levaditi, syphilis of the ovary is a very rare occurrence.[21] Warthin[231] said that in thirty-five years of pathologic study he had never seen a lesion in this organ which he could call syphilitic.

It is conceivable, as Lombardo[139] has pointed out, that treponemes could traverse the decidua reflexa from the time of nidation to its closing with the decidua serotina, especially since treponemes have been found in the cervical canal after intercourse with syphilities. And, since they have been demonstrated in the chorion (Mohn) and in the decidua (Trinchese[219]) this theory would accord with the absence of spirochetes in early abortions in which the mother is not infected;[112] but this mode of transfer has never been proved. There remains the transplacental route. The infectiousness of the blood in latent syphilis has been shown by Uhlenhuth and Mulzer (Berl. klin. Wchnschr. **50**: 769, 1913). The mode of passage from the maternal to the fetal circulation has been variously explained and is probably not always the same. Most usual, perhaps, is the formation of an infected embolus, which gives rise to a small infarct in the placental blood vessels, through the walls of which the spirochetes may grow, much as they grew through the Berkefeld filters in Noguchi's experiments with them in artificial culture media. That no histologically demonstrable lesion is necessary for this transfer to take place, however, has been shown by Trinchese[219] who found that ''in small veins the individual spirochetes were able to pierce the vessel walls without causing visible injury.'' Larger numbers of spirochetes ruptured the vessel wall in order to enter the blood stream. A third

mode of transfer has been suggested by Rietschel[182] who feels that, in the majority of cases, it is unlikely that the spirochetes can pierce the thin intima and adventitia of the blood vessels, but gain access to the fetus by their own locomotion through the perivascular lymph channels of the umbilical vessels. The reason that the spirochetal invasion of the fetus does not take place early finds, theoretically, a ready physiologic explanation, for it will be remembered that it is only after three or four months of pregnancy have passed that the cylindrical Langhans cell layer commences to atrophy and that it is not until the sixth month that it can no longer be detected. From this time on, the spirochetal invasion is at its height, a very important protective layer having been removed (Kristjansen,[126], Hoffmann,[106] Trinchese,[219] who found spirochetes penetrating Langhans cell layer in only 1 per cent of the cases). Death of the fetus, when it occurs, is said to result from a failure of adequate blood supply through a closure of the placental vessels (McCord,[144], Browne[40]). It should be borne in mind, that for syphilis to be present in the fetus, spirochetes must have passed over the placental barrier, and the mere detection of syphilitic lesions on the maternal side of the organ does not necessarily mean fetal syphilis, though this is usually true. Almost any large series of cases will show a few instances in which the placenta was diagnosed syphilitic, but the child remained symptom-free and serologically negative (Williams[240]).

We may with some reasonable assurance conclude, then, that infection of the ovum before rupture of the follicle does not occur. Equally improbable is the infection of the ovum in its passage from the ovary to the uterus. In rare instances treponemes invading the uterine cavity from infected semen may traverse the decidua reflexa. But, it is proved that whether preconceptional or postconceptional syphilis is in point, transplacental invasion is the habitual route, especially in the latter half of pregnancy (for another viewpoint in this question see Schamberg and Wright[195]).

Effect of Pregnancy on Syphilis.—From the standpoint of diagnosis, a problem of equal importance with that of the manner of fetal infection is the question of the effect of pregnancy on maternal syphilis. The fact that syphilis is apt to run a rather benign clinical course in women was a very early observation (Swediaur,[216] p. 296), and forms the basis for Colles' well-known law.[48] Even in 1810, Bertin[22] (p. 63) attributed part of this effect at least to parturition, when he remarked, in speaking of the symptoms of the disease in pregnant women, "the pregnant state modifies them and causes them sometimes to disappear spontaneously." The rôle played by pregnancy in producing latency or regression of the disease has been restudied in the last twelve years, experimentally in animals by Brown and Pearce,[37] and Chesney,[47] and clinically by Moore,[159, 160, 161] Solomon,[204, 205] Stokes[211, 212, 213] and others. In 1920, Brown and Pearce found that, of 8 pregnant female rabbits inoculated with strains of *Treponema pallidum*, only four of them showed any clinical sign of infection, whatsoever, and in three of these, the reaction consisted of a slight transient infiltration. Five nonpregnant females and three males inoculated with the same material at the same time all developed typical lesions. That this work is not absolutely conclusive, however, is shown by the subsequent experiments of these same investigators,[38] when they demonstrated the penetration of the normal mucous membrane of the rabbit by *Treponema pallidum*, without a local reaction developing. Likewise Chesney[47] found that five nonpregnant females developed an intradermal reaction approaching closely that "exhibited by the pregnant animals" in the foregoing paper and concludes that the "behavior of any one group of rabbits toward infection with the *Treponema pallidum* is by no means indicative of what may be expected subsequently in another group of animals even if infected with the same strain." The clinical studies, likewise, purporting to show the ameliorating effect of pregnancy upon the course of the syphilitic infection

are not entirely free from criticism. For example, even though, in the out-patient department, it was possible for Moore[160] to show that latency was almost twice as common in women as in men (24 per cent as compared with 47.5 per cent), of the 1085 women with Wassermann positive latent syphilis 470 (43.3 per cent) were pregnant at the time of the first observation (Turner[223]). The incidence of latency, and indeed of symptomless or almost symptomless syphilis in the population at large is very difficult to determine (Fordyce[74]), and most of these women would have remained undiscovered had not a routine of Wassermann reaction on all pregnant patients been done. The incidence of latency among males might be found to be nearly as great, did pregnancy attract as much attention in their behalf. On the other hand, both clinically and pathologically (Wile,[236] Warthin[231]) latent syphilitic women seem extraordinarily free from many elective signs of syphilitic disease in heart and blood vessels, as well as in the parenchyma of the cord and brain,[159, 160, 205, 26] as compared with men (Abraham,[1] Hemsath,[101] Pillsbury,[174] Roberts[185]). That pregnancy is the biologic agent causing this picture is not yet demonstrated.

A number of writers both in this country and abroad feel that pregnancy causes an impetus to the multiplication of spirochetes and a recrudescence of clinical symptoms, and when one considers that the usual effect of pregnancy on chronic infection is detrimental to the mother, this view must be given at least some credence. Fournier[78] (p. 725) has called attention to the marked increase in size and severity of local primary or secondary lesions of the genitalia which may occur in pregnancy (Boas and Gammeltoft[30]). Recent observations[88, 134, 154, 137] point out numerous instances in which malaise, general ill health, headaches, greater tendency toward toxemia, have been attributed to the presence of this disease and Bertin[23] reports a case in which hepatic syphilis and hemiplegia, and another in which tertiary skin lesions appeared during pregnancy. It is interesting to note also in Moore's series[160] that although the disease seemed milder than one might otherwise expect, 35 of his pregnant women had primary or secondary syphilis on admission, and of 18 primiparas, followed for two or six years, in 7 there was definite evidence of progression of the disease. Four of these had aortitis, one had syphilis of the liver, another a positive cerebrospinal fluid and the last a definite neurorecurrence. To look at the question from a slightly different viewpoint, in any series of pregnant women there will be found a few cases in which the Wassermann reaction, positive during pregnancy, becomes negative after delivery[15, 31, 49, 54, 123, 210, 240] and occasional cases in which the reaction negative early in pregnancy becomes positive at term.[142] While there are those who have considered these tests as evidence of a nonspecific positive reaction developing as a result of the blood change in the woman during pregnancy, these women can often be shown to be syphilitic (Kolmer,[123] p. 469). In all probability the effect of pregnancy on the syphilitic infection in the gravid woman is, in most instances, not sufficient to make any appreciable difference from the purely diagnostic standpoint.

While we are dwelling upon the effect of syphilis on the pregnant woman, it might not be out of place to inquire into the effect of the disease upon labor and upon maternal morbidity during the puerperium. In a general way we may say that in this respect likewise the differences between the syphilitic and the non-syphilitic woman are not very marked. In rare instances malpresentations owing to prematurity or maceration of the fetus may cause difficulty.[185] Uterine inertia, impediment of labor because of a "wooden" cervix, or fibrosis of the birth canal from previous lesions have been described.[154, 185] Infrequently, subinvolution of the uterus has been attributed to this disease.[166] Syphilis does not play an important rôle in the causation of puerperal sepsis or maternal morbidity. Boas and Gammeltoft[30] in a series of some 12,000 parturients found a maternal morbidity of 20 per

cent for the syphilitic group (528 cases) and of 19.4 per cent for the nonsyphilitic (11,844 cases). Toland's figures (218) for 500 cases at the Pennsylvania hospital are 30.7 per cent and 25.2 per cent respectively.

Diagnosis of Syphilis in the Mother.—It might be expected from the foregoing that the value of a clinical history and a physical examination in diagnosis of syphilis in the infected mother would be extremely low in most instances. While it is unsafe to rely totally on this means of investigation, evidence suggesting the presence of the disease is found in a surprisingly large number of cases. From the history and physical examination alone, the diagnosis can be made in from 25 per cent to 64 per cent of the cases (Boas and Gammeltoft,[32] 57 per cent, Moore,[160] 35 per cent, Dodd,[62] 64 per cent, Browne,[39] 25 per cent). History of primary or secondary symptoms probably never exceeds 20 per cent of the cases and of course varies considerably with the intelligence of the patient and the age of the disease (Beck[15] gives 6.7 per cent; Goodman[91] 10 per cent; Jeans[109] 13 per cent; E. R. Hall[97] 15 per cent; Halloran[98] 19 per cent). The presence of detectable physical signs, likewise, is in accord with the type of material, but, in general, here again, between 10 and 20 per cent will show some evidence of the infection (Halloran[98] 7 per cent, Beck[15] 12.5 per cent, Moore[160] 18 per cent). That such signs are more likely to be present early in the disease is shown by the studies of Belding[20] which revealed an incidence of 29.7 per cent in seropositive, and only 12 per cent in seronegative cases. The importance of always examining thoroughly is pointed out by Welz and Van Nest[234] who, in 147 proved syphilitic pregnant women, found that 19.7 per cent had syphilitic skin lesions, 28.5 per cent absent or markedly retarded reflexes, 12 per cent Argyl-Robertson pupils, and 50.3 per cent generalized adenopathy.

As the age of the disease increases and the occurrence of the serologic evidence thus decreases, the value of the obstetric history plays an increasingly important part. In general, between 50 and 60 per cent of multiparous women will give a positive history of sterility, abortions, miscarriages, deaths in infancy, or syphilitic children (Beck[15, 16] 62 per cent; Belding[20] 40 per cent; E. R. Hall[97] 80 per cent; Halloran[98] 59 per cent; Solomon,[204] p. 120). Roy H. Turner[222] of Tulane University found that, of 42 patients with clear-cut tertiary syphilis, 57 per cent gave a history of stillbirths and only 45 per cent had positive Wassermann reactions, and concluded that pregnancy may be looked upon as a test for syphilis comparable to the Wassermann reaction in the multipara. The fact that, in his series of 388 cases, the greatest incidence of syphilis was between thirty and forty years, likewise again points out the fact that it is in the multipara rather than in the primipara that we must be most on our guard. As mentioned above, the occurrence of repeated early abortion is not of much diagnostic value and will usually prove not to have a syphilitic etiology. But, as might be expected from the fact that the transfer from mother to child through the placenta may take place as early as the fourth month, the incidence of abortion before the twenty-eighth week is slightly higher in the syphilitic than in the nonsyphilitic group, when parallel series are run (Bartholomew[14] and Corda[51]). To be noted in this connection are those cases of abortion starting as early as the third month which have been successfully treated by antisyphilitic therapy (Jensen-Carlén[112]), and the few instances in which the treatment of paternal syphilis alone has caused the birth of a healthy child (Moore[160]). Prematurity, while not characteristic of syphilis, will usually occur in upward of 20 per cent of cases (McCord,[141] Moore,[160] Corda,[51] Cruickshank,[54] Klaften[120]). Though maceration of the fetus is an item rarely obtainable from the history, it is considered to be highly indicative of syphilis, occurring in, perhaps, 45 per cent syphilitic prenatal deaths (McCord,[143] Holland and

Lane-Claypon,[107] Cruickshank[55]), while about 80 per cent macerated fetuses are considered to be syphilitic (Williams,[238] Lasseur and Vermelin,[129] Morosoff and Raskin,[162] Palmer[169]).

In connection with a consideration of the effect of syphilis on the fetus, it is well not to place too much diagnostic, prognostic, or therapeutic import on the fact that the disease may become less active as it ages and that subsequent pregnancies are apt to result in the birth of healthy children. It was a very old observation (Diday,[61] p. 137) that the syphilitic infection wears out and exhausts itself upon the first children, so that we have, in succession, severely diseased embryos which succumb to the affection within the uterus, children which are viable but which give distinct evidences of syphilis, those who become ill to a very slight extent only and relatively long after birth, and, finally children born alive free from syphilis (Kassowitz' law[116]). In about 50 per cent of the cases the disease will be most marked in the earlier pregnancies, but in almost as many cases children apparently free from infection will crop up irregularly in the midst of definitely syphilitic children and miscarriages (Jeans,[109] Jewesbury[113]). The following authors have reported cases illustrative of the foregoing statements. The first published in 1810, by Bertin is a perfect example of Kassowitz' law formulated in 1876; the others show the common types of exceptions which may be expected.

TABLE II

NUMBER OF PREGNANCIES	1. BERTIN[22]	2. WILSON[242]	3. FOURNIER[78]	4. GAMMELTOFT[85]
1.	Miscarriage—6 months	Miscarriage—6 months	Abortion—5 months	Stillbirth
2.	Miscarriage—7 months	Miscarriage—8 months	Premature—7½ months, lived 15 days	Sound child; healthy at 15 years
3.	Miscarriage—7½ months	Premature, lived 7 days	Stillbirth at term	Child died of cong. syphilis
4.	Full term, lived 18 hours	Abortion—3 months	Stillbirth—7½ months	Stillbirth
5.	Full term, lived 6 weeks	Abortion—3 months	Stillbirth—premature	Abortion
6.	Full term, lived 4 months	Lived 14 months	Abortion—3½ months	Healthy child 8 years old
7.		Abortion—2 months	Abortion—6 months	Healthy child 7 years old
8.		Stillborn at term		Death in infancy
9.				Abortion
10.				Healthy child 4 years old
11.				Death in infancy
12.				Died of cong. syphilis

Thus, while this law represents a general tendency, it cannot be expected to be fully exemplified in any given case (see also Browne,[39] Abraham,[1] Solomon,[204] Lees,[134] Belding[19]). The birth of living syphilitic children suggests another di-

agnostic aid, applicable in a small number of cases, namely, the examination of other members of the family when the presence of the disease is questionable in the mother. Beck[16] found that in 33.8 per cent of multiparas other children in the household had syphilis. Belding and Hunter[20] felt this type of evidence was of value in 10 per cent of cases and they were able to obtain a history of syphilis in the husband in 20 per cent of cases.

In instances where the infection is comparatively recent the most valuable diagnostic aid is the serologic examination. That it should be carried out in every pregnant patient is shown very well by the work done in Boston,[18] where, in 5000 maternity patients who were examined routinely without especial attention to syphilis, definite clinical evidence was obtained in only 0.54 per cent and suspicious signs in 1.7 per cent, a total of 2.2 per cent, whereas the Wassermann test in the same group was positive in 9.2 per cent. In Philadelphia, in 1931, the incidence of syphilis was about 5 per cent in 25 prenatal clinics making routine serologic studies, and it was only 1 per cent in 11 clinics employing the test merely as indicated. When the Wassermann test first began to be generally employed, the high percentage of positive reactions occurring in a series of pregnant women was so surprising that many writers felt there must be a nonspecific test which arose often as a result of some obscure blood changes occurring in connection with parturition. The fact that these women were so often symptom-free, that there were marked variations in the strength of the reaction during pregnancy,[101, 160] that the reaction negative in the early months might become positive at the time of labor,[142] and that not rarely a reaction positive during pregnancy became negative after confinement[15, 31, 49, 54, 123, 210, 240] seemed to add weight to this point of view. Some experimental evidence forces the same conclusion. This, Esch and Wieloch,[68] in a series of 777 women reputed to be free of syphilis found so-called nonspecific positive results in about 8 per cent complement fixation and about 1.5 per cent precipitation reactions during the latter months of pregnancy. Strepowski[215] in a series of 618 serums found apparent nonspecific serum reactions in about 1 per cent cases. Stillians,[210] in this country, found disagreement in some 5 per cent (see also [165a]). In such instances it is, at times, almost impossible to prove or disprove the presence of syphilis in the individual in question, at least during a short period of observation. The current consensus of opinion in this regard is that nonspecific positive reactions do not occur during the early months of pregnancy; that they appear only rarely in the latter months, if they exist at all. (Kolmer,[123] Kilduffe,[118] Stillians,[210] Spiegler,[207] Boas, Gammeltoft and Siecke.[32]) In order to avoid all diagnostic error, it is recommended[215] that the examination of the serums of women under suspicion be carried out by the greatest number of diagnostic procedures possible. When all furnish a positive result, there is room for serious suspicion of the presence of a syphilitic infection. When positive reactions occur in unsuspected cases, the test should be repeated as soon as possible, for, while statistics tend to minimize error, in dealing with an individual the matter is entirely different because a mistake here means an error of 100 per cent (see Solomon,[204] p. 142).

The value of retroplacental blood in the diagnosis of syphilis in the pregnant woman during labor has interested European writers since the work of Opitz in 1908 (see Bruno[41]). While the most recent workers,[207, 243] by using more refined technics report better results than were formerly thought possible, nonspecific positive reactions do occur in an appreciable number of cases.[29, 31, 41] It has been suggested by Lesser,[138] however, that a negative reaction obtained in the retroplacental blood might render future study of the mother's serology unnecessary.

The use of umbilical cord blood to diagnose syphilis in the child at the time of birth is apt to give such a variety of results, often defying interpretation, that its use has been abandoned in a number of the larger clinics in this country, today.

The difficulty arises from the fact that, whereas complement fixing substance may be formed in both the mother and the child, the placenta, ordinarily impervious to the transfer of this substance (see Nakayama,[165a]), is sometimes rendered patulous through trauma at the time of birth, so that there may be a free interchange between the maternal and fetal blood (see experiments of Aron [Compt. rend. Soc. de Biol. 100: 824, 1929]). Indeed, at times, according to Rietschel,[182] we have to do with maternal rather than fetal blood in the cord. Another complicating factor rests in the observation that a negative cord Wassermann does not exclude syphilis in the child, for it is a well-known fact[4, 11, 75, 186, 233] that a syphilitic infant often does not develop positive serology for several weeks or months after birth. Table III shows the combinations of maternal and fetal syphilis which are to be found in the literature.

TABLE III

	SYPHILIS IN MOTHER	SEROLOGY IN MOTHER	SEROLOGY IN CORD	SYPHILIS IN CHILD	OBSERVERS (REFERENCES)
1	+	+	+	+	55, 75, 101, 111, 165a, 198
2	+	+	+	−	30, 34, 54, 64, 70, 72, 75, 101, 135, 138, 155, 182, 217
3	+	+	−	+	4, 11, 75, 186, 233
4	+	+	−	−	55, 101, 198
5	+	−	+	+	1, 155, 198
6	+	−	−	+	138, 141, 186
7	+	−	−	−	241
8	−	+	+	+	138, 182
9	−	−	+	−	186
10	−	−	−	−	

From this it will be seen that, so far as diagnosing the presence of syphilis in the child is concerned, the cord Wassermann is of little value unless the maternal Wassermann at the time of birth is also determined. A positive cord Wassermann, on the other hand, is usually indicative of the presence of active syphilis in the mother, at least, and it has been demonstrated that the child is much more likely to be infected in such an instance.[30, 217, 20] Furthermore, if the cord Wassermann is positive in the presence of negative serology in the mother, the child is almost certainly syphilitic, the few cases in which laboratory technic or the so-called nonspecific reaction of pregnancy are at fault being excluded (see Lemež[135]). In his recent publication Abraham[1] found two such cases in a series of 94 syphilitic pregnant women. When the disease is not discovered in the mother before the birth of the child it cannot be detected in the infant early unless his blood is examined, and it has been repeatedly pointed out that the treatment of congenital syphilis after it has become manifest is, at times, an extremely unsatisfactory procedure.[226, 229] Kilduffe[118] (p. 94) is of the opinion that a positive cord blood reaction, if it has no other value, "is at least an indication for further and prolonged study of the case."

Diagnosis of Syphilis in the Child.—If the child has a positive reaction in its blood at the time of birth, caused by a transfer of complement binding substance from the mother, without a spirochetal infection resulting, this test will rapidly become negative after birth and seldom exists longer than ten to fourteen days.[9a, 30, 34, 64] When the reaction is negative at birth in spite of the presence of syphilis in the child, it will ordinarily become positive in the course of six or eight weeks,[9a, 138] though in rare instances the change does not appear for several months or even years after birth. The fact that the mother's blood is negative to the Wassermann test throughout pregnancy does not necessarily mean that the child will

be free from the disease, as has been previously stated. Therefore, every effort must be made to diagnose syphilis in suspected cases clinically as well as serologically. In general, the serologic evidence will antedate the appearance of definite signs by some weeks or months.[186]

From the clinical standpoint, the diagnosis of the disease in the child commences with the examination of the placenta and cord immediately after birth. In this connection, it is well to recall that nothing short of the demonstration of treponemes in the fetal circulation of that organ is indicative of a positive diagnosis of syphilis in anyone but the mother, though much suggestive evidence will often be obtained to establish this point. The textbook description of the syphilitic placenta, pale, greasy, bulky, is found only in the cases where the fetus has died before birth and is macerated.[40] Unless the disease is so far advanced that the child is obviously syphilitic at birth, the placental changes will not be marked enough grossly to be detected from the normal appearing organ. Mraček,[164] in 1903, could not detect more than 47 per cent of the average run of cases in this manner (see also Slemons[203]). The normal placenta at term weighs less than one-fourth the fetal body weight. If a placenta weighs more than one-fourth the body weight it is almost certainly syphilitic. A placenta, however, with a normal weight ratio does not necessarily exclude syphilis. This criterion has been found to be of value in 25 to 50 per cent of cases (Duca and Geyer,[63] Browne,[39] Slemons,[203] Lasseur and Vermelin.[129] The microscopic study, preferably of a stained section, is of more value. The changes here seen and first described in 1873 by Fränkel,[83] consist of a proliferative inflammation commencing in the walls of the smallest blood vessels, resulting in extensive infarction, so that the chorionic villi, which show a decrease in the usual dichotomous arrangement, are thickened and irregular in size, the ends of many exhibiting a distinct clubbing and a marked decrease in vascularity. Slemons[203] in 1917, found, in a comparative study of the Wassermann reaction and placental findings, in 360 consecutive confinements, that the tests agreed absolutely in 95 per cent of obstetric patients. The demonstration of the microorganisms themselves in a syphilitic placenta is much more difficult, ordinary procedures yielding about 33 per cent positive results,[203] though they can be found in as high as 80 per cent of cases as Trinchese has shown[219] by making 200 to 250 silver stained sections from each organ. Finding spirochetes, or, indeed, any evidence of the disease in the umbilical cord, is not possible in more than 10 to 20 per cent of cases.[219, 67] Enlargement of the liver, spleen, and lymph glands, during the first few weeks of life, while often an accompaniment of the syphilitic infection in the child, are neither typical nor dependable.[39, 40, 135, 186, 226] In untreated cases, the typical skin lesions and rhinitis will make their appearance by the end of the second month in about 80 per cent.[61, 186, 226]

The only other procedure in general use applicable to the living child is the examination of the long bones by means of the roentgen ray for evidences of syphilitic osteochondritis, first described grossly by Wegner.[232] Pendergrass and Bromer[173] feel that the roentgen appearance of the osteochondritic process is characteristic and scarcely to be mistaken for any other condition (see also Shipley, Pearson, et al.[202]). The most important diseases to be differentiated from it, rickets and infantile scurvy, rarely occur before the fourth month, and Roberts[186] has recently observed that it was one of the most striking features of osteochondritis in the syphilitic infant that it was most often found in the second or third month of life, he having seen no case in which it appeared after the fifth month. McCord[143] states, "My studies would seem to show that the lesions in the bones are almost pathognomonic of fetal syphilis and, with the exception of finding the organism in the stained tissue, are the most reliable aid. It is the one single examination that can be made almost anywhere, and the results of which are easily interpreted and

thoroughly reliable.'' In a series of 59 babies[147] he found the roentgenograms were positive and the placentas negative ten times, and that the placentas were positive with negative bone lesions in three cases (see also McCord,[146] Adair[3]).

It should be evident by now that the diagnosis of syphilis in the mother or in her child after birth is no easy matter, if you would approach a 100 per cent accuracy. It requires a knowledge not only of the mechanism of infection, which is usually transplacental; not only an understanding of the peculiarities of syphilis in the woman, and more particularly in the pregnant woman, where it is most often, for reasons not as yet understood, in the almost symptomless latent stage; it requires, in addition, a certain finesse in history taking which will bring to light the unpleasant and often easily forgotten memory of an old venereal disease. It involves more than a cursory physical examination of the woman, and a blood test. It necessitates an evaluation of the symptoms found, an interpretation of the serologic findings, in some instances quite confusing, an examination of the placenta, as thorough as possible under the circumstances of the delivery, and a physical examination and serologic study of the child. Even then an occasional case may escape detection, unless the follow-up is ideal.

Treatment of Syphilis in Pregnancy.—The treating of the syphilitic mother to preserve her child is reputed to have been first advised and carried out in France in about the middle of the seventeenth century.[22, 227] At this time Garnier, because syphilitic pregnant women were refused admittance to the lying-in hospitals at Paris, proposed to house them in a separate hospital, feeling that, contrary to the then current opinion, treatment with mercury rubs, even to the point of salivation, far from harming gravid women, would cure them and their children. Mauriceau,[153, 206] living in this period, recognized the value of the proposal and reports the birth of healthy children as the result of mercurialization carried out during pregnancy. This mode of treatment was used, more or less, by the French all through the eighteenth and nineteenth centuries (Astruc,[9] Mahon,[149] Swediaur,[216] Doublet, mentioned by Bertin[22]), and, even until fifty years ago, its strongest advocate was the elder Fournier.[77, 78, 79, 80] The results they obtained were not as good as one could expect from the use of mercury today, because most of the cases were seen only late in pregnancy, but still, approximately 40 per cent of the children of pregnant syphilitic mothers were discharged in apparently healthy condition (see Bertin). Prophylactic treatment of congenital syphilis first began to be used in this country between 1870 and 1880, three case reports of the effectiveness of the use of mercury to prevent abortion in the syphilitic woman having appeared in the American literature in this decade.[114, 133] G. K. Johnson (1877) writes, after describing two successful instances of the administration of mercury, ''These two cases show, as far as two cases can show, the advantage to the child of such medication, addressed to the mother during gestation, and they teach the practical lesson, that under such circumstances we ought diligently to use remedies in the hope that we may thereby save the child from a deadly inheritance.'' That this type of treatment has not completely lost its usefulness is shown in Cook's recent report in the *British Medical Journal*,[50] where, after remarking that approximately 80 per cent of the natives of Uganda suffer from syphilis, he says: ''There are records of innumerable cases of women who, after long series of miscarriages, bore healthy children for the first time after a course of this (mercury) treatment, which is rapidly increasing in popularity; husbands often make a journey of many miles to obtain it for their wives who are unable to walk the distance.''

The advent of the arsphenamines has increased the number of nonsyphilitic children of infected mothers from something in the neighborhood of 30 per cent[30, 85] to a figure which approaches 100 per cent. At least one small series of cases has been reported in which, as a result of adequate treatment of the mother during

pregnancy, not a single syphilitic child was born (Greenlees[96]). With such results as these, congenital syphilis can, in the opinion of many European and American investigators, be practically eradicated (see Pillsbury[174]). Many clinicians report series of cases in which the number of living children obtained exceeds 85 per cent (Boas and Gammeltoft,[30] Wile and Shaw,[237] Williams,[241] Stacy,[209] Richter,[180] Pye-Smith,[177] Marshall,[152] McCord,[146] Lesné and Linossier-Ardoin,[137] Laurent,[130] Kristjansen,[126] Klaften,[120] et al.).

The manner in which antisyphilitic therapy prevents the spread of the infection from the mother to the child is still somewhat a matter for speculation. That mercury,[45, 46, 167] bismuth[125] and arsenic[167, 125, 225, 60] traverse the placental barrier, in small quantities at least, has been shown by various investigators. Many workers feel, however, that with the therapeutic doses of the drug usually employed in treating syphilis in the pregnant woman, the amount of metal which gains access to the fetal circulation is so slight as to be of little therapeutic value. Thus, Underhill and Amatruda,[225] at Yale University, experimenting with rabbits found that arsenic could be detected in the fetus, after intravenous injections of neoarsphenamine into the maternal circulation, in small traces only, and the amount of arsenic recovered from the fetal tissues did not increase in proportion with the number of serial injections given. Eastman[65] at Johns Hopkins found no arsenic in the umbilical cord blood, nor in the liver or kidneys of a stillborn fetus. Meyer,[156] likewise, reports that arsenic is seldom found in the fetus following treatment of the mother. Other workers[2, 136, 168] have had difficulty in demonstrating the presence of bismuth in the products of conception. Many of these investigators, however, have found the metals stored in unusually large quantities in the placental tissues, and it is possible that the drugs administered to the mother act more by preventing spirochetemia and by destroying the treponemes at the portal of entry, than they do by any therapeutic action in the newborn child. As Eastman and others have pointed out, arsenic deposited in the tissues is not necessarily therapeutically active, but certain it is that treatment begun late in pregnancy is many times less effective than therapy instituted soon after conception. Thus, in Richter's[180] series of 746 cases, in those in which the treatment was started in the second, third, or fourth month of pregnancy, none of the children were syphilitic; when not treated until the fifth or sixth month between 35 per cent and 40 per cent were syphilitic; and those who commenced active therapy during the seventh or eighth month gave birth to infected children in three-fourths of the cases. Other workers have reported similar results.[146, 152] It would seem, then, that once the fetus is infected, the chances of obtaining a nonsyphilitic child at term are not very good, though treatment begun late in pregnancy will probably decrease the liability of occurrence of a miscarriage or stillbirth, and thus enhance the opportunity of curing the child postnatally.

The treatment of syphilis during pregnancy, like the treatment of syphilis under any other condition, is a much debated question. It is, perhaps, more than a coincidence that the only arsphenamine death occurring in the University of Pennsylvania Hospital in a series of 17,000 injections of the drug, was in a pregnant woman. Kristjansen[126] calls attention to the fact that, of all the patients treated with salvarsan at Rudolph Bergh's Venerological Hospital, during the ten years prior to 1927, four died of salvarsan poisoning and three of these were pregnant women. Gougerot[94] reports one death in 9,000 cases following the use of arsphenamine in pregnancy. Arsenic intolerance, without being fatal to the pregnant patient, may cause detectable liver damage,[132] kidney damage,[15] or even premature labor[98, 10, 92, 93] in addition to the more common nitritoid crises and gastrointestinal disturbances. While bismuth is not quite as dangerous to the mother in this respect,[93] it is not nearly so effective as a therapeutic agent in preventing fetal

syphilis,[28, 57] though some favorable results are reported.[2, 194] Wile and Shaw[237] say: "We feel that in view of the extra burden of pregnancy thrown upon the parenchymatous organs of the mother, ever a greater attempt in treating the patient rather than the disease should be made, than is advocated for the treatment of syphilis alone. For this reason rigid criteria of treatment should be avoided and each patient considered as a therapeutic problem, to be solved according to the indications and contraindications." The danger is not great if reasonable care is taken.[212, 237, 180, 1]

It has been advised that the pregnant woman be treated on the mere suspicion of syphilis,[75] that the expectant mother be treated if her husband has had syphilis,[13, 79] and that a woman who has once been shown to be definitely diseased, be treated in all her subsequent pregnancies, regardless of previous therapy.[13, 29, 30, 40, 85, 148, 152, 207, 212] It is doubtful if the pregnant woman should be subjected to treatment, without the existence of the disease in her having been definitely established, any more than the nonpregnant would be.[29, 77] The answer to the last question is not to be had until we learn more of the curability of syphilis under a modern therapeutic régime. Birnbaum[27] reports a series of 21 women in whom a previous syphilitic infection was cured by appropriate treatment. They later had 34 pregnancies, untreated all the while, which resulted in apparently normal children, who have remained free of syphilis, some for as long as six years (see Zieler[248]). In the present state of our knowledge, a mild course of treatment during pregnancy in these cases, when not otherwise contraindicated, might make the birth of a nonsyphilitic child more certain.

The treatment of the child of the syphilitic mother, on the other hand, should not be commenced before the diagnosis of the disease in him has been established. Solomon[204] (p. 42) has shown, in examining the living children of 236 syphilitic women that 72.5 per cent of them were free of any evidence of the disease. Fordyce and Rosen[75] pointed out the fact that "infants of treated mothers have now been followed serologically for years with negative results." That such children should be subjected to therapy for the sake of their diseased brethren, is neither logical nor scientific, especially when the mother has undergone adequate treatment during her pregnancy.[29, 64, 85, 165, 186] If the mother has early syphilis and has received little or no surveillance during parturition, the chance of her offspring being infected is more than 85 per cent. Under such circumstances some authors feel justified in instituting treatment in the child without consuming time in attempting to make a diagnosis.[9a, 134] Especially to be cautioned against, is the practice advocated by some,[9a, 237, 15] of treating infants of syphilitic mothers for a few weeks after birth, and then dismissing them, with or without periods of observation, if they remain symptom-free. Such a procedure would succeed in curing only those infants who did not have the disease, and would give a false sense of security to those cases who are harboring the microorganism. It is, of course, unwise to commence treatment on finding a positive cord Wassermann alone.[64, 186]

The problem of treating the child by the old Hippocratic method, via the mother's milk, has been recently raised again by Campbell and Frost[42] of Los Angeles. That the mother's milk contains an appreciable amount of arsenic while she is on active therapy, has been shown by Fordyce, Rosen, and Myers,[76] and this may be absorbed by the gastrointestinal tract, as Kolmer and Schamberg have shown.[124] These latter workers have demonstrated, also, that the therapeutic action of arsenic received in this manner is very slight, and it is probable that few would advocate this method of treating active infantile syphilis. The question of the syphilitic mother nursing her own child has appeared, in the past, more as a theoretic than a practical problem, but it should be borne in mind that the infectiousness of the mother's milk during the active stage of the disease has been

shown by Uhlenhuth and Mulzer,[224] and Gougerot[95] has recently again called attention to possible exceptions of Colles' Law, saying that he is personally acquainted with two cases in which syphilitic lesions of the mother's nipple have developed through her nursing her syphilitic offspring.

The management of syphilis in pregnancy, once the diagnosis has been established, consists, then, in the treatment of the pregnant woman with an arsenical and a heavy metal, in much the same manner that a nonpregnant woman is handled. The increased strain of pregnancy upon the maternal organism renders her slightly more susceptible to the various types of drug intolerance which are apt to develop under a rigorous arsenical régime, and urge some caution in the application of the treatment.

The question of treating a syphilitic woman in all her pregnancies, regardless of previous therapy is an open one, the answer to which depends upon personal belief as to the curability of syphilis, but the weight of authority and conservatism suggests a prophylactic course of treatment following each conception.

The newborn child should not, except perhaps in a few rare instances, be treated before diagnosis is made—as in any adult case of syphilis, and when therapy is commenced, it should be as prolonged as would be given to any syphilitic patient, this especially being the case since treatment of the mother, in all probability, prevents rather than cures fetal syphilis.

SUMMARY

Syphilis in the latent stage, as it exists in most pregnant women, is difficult to detect. This means that the disease must be suspected in every case, for a successful termination of pregnancy and a healthy child cannot be expected in the presence of an active or even a quiescent infection of this nature.

The incidence of syphilis among pregnant women in the clinic class of patient is usually between 5 and 10 per cent. It occurs probably less frequently in the higher classes but, because it is less often looked for, more cases are likely to escape detection. In the presence of a comparatively early untreated syphilitic infection the infant mortality rate is increased to five times the accepted average.

Most authorities agree that syphilis runs a milder course in women than it does in men, but it has never been conclusively shown that pregnancy is the biological agency responsible for this change. There is some evidence that the disease may be activated by the added strain upon the maternal organism during parturition.

None the less, when the history and physical examination of the expectant mother are completed, one should be able to suspect the presence of the disease, if the woman is infected, in from 25 per cent to 64 per cent of cases, but in no instance should the blood serum Wassermann reaction be omitted. Since patients with infection of long standing, and those inadequately treated may give birth to a syphilitic child in the presence of a negative serologic examination, every child born deserves the benefit of a study to rule out this disease. In addition to the usual procedures, the umbilical cord blood is of value if all findings are properly interpreted and in this connection roentgenologic studies of the long bones are both reliable and valuable. It is wise to follow suspicious cases for some months at least.

The results obtained by early treatment of the syphilitic mother to save her child are scarcely paralleled in any other medical condition. An infected offspring is seldom encountered if therapy has been commenced prior to the fourth month of pregnancy. The observation that the Treponema pallidum does not traverse the placental barrier early, and the fact that antisyphilitic drugs, only with great difficulty, penetrate the membranes separating the maternal and fetal circulation, together emphasize the urgency of preventing infection of the child while there is

yet time. For, once the microorganism has gained access to the fetal circulation, it is improbable that the fetus will be cured while still in the womb.

On the other hand, nonsyphilitic children, especially after adequate prenatal treatment, result with sufficient frequency to make one feel that the offspring should practically never be treated until the disease in him is demonstrated. This viewpoint is further strengthened when one considers the prolonged course of active therapy with relatively toxic drugs that is necessary to insure a clinical cure of any syphilitic patient. Treating an infected child for a few weeks postnatally cannot be expected to eradicate this disease.

In general, the pregnant syphilitic woman can undergo the same type of treatment régime as can the nonpregnant, but the technic of administration of the medication must be above reproach, and the dosage and type of drug gauged according to the condition of the patient.

Too often, in the past, when the physician practicing obstetrics or pediatrics has lost a child suffering from syphilis or has permitted the disease to become clinically manifest before treatment was instituted, the responsibility for the unfortunate outcome has been placed upon the patient's lack of cooperation. In the present state of our knowledge the most careful diagnostician may fail to detect an occasional case, but these failures should be very rare indeed. It is to be hoped that the future instances in which syphilis is not diagnosed in the pregnant woman or in her offspring will be those few in which the disease escaped detection although every available method for revealing its presence had been employed.

REFERENCES

(1) *Abraham, J. Johnston:* Brit. M. J. **2:** 237, 1932. (2) *Abruzzese, G.:* Riv. ital. di ginec. **10:** 381, 1929. Abst. Cong. Syph. U. S. Public Health Service, U. S. Govt. Print. Office, Wash., 1930. (3) *Adair, Fred L.:* Am. J. Obst. & Gynec. **23:** 111, 1932. (4) *Adams, J.:* Lancet **2:** 990, 1920. (5) *Idem:* Brit. Med. Jour. **1:** 56, 1922. (6) *Idem:* Lancet **2:** 174, 1929. (7) *Almkvist, J.:* Abst. Cong. Syph. U. S. Public Health Service, U. S. Govt. Print. Office, Wash., 1930. (8) *Armstrong, I.:* Public Health Nurse **21:** 574, 1929. (9) *Astruc, J.:* A Treatise of Venereal Diseases in Nine Books, Translated from the Latin by William Barrowby, Jr., London, 1754. (9a) *Atlee, E. D., and Tyson, R. M.:* Am. J. Dis. Child. **44:** 718, 1932. (10) *Audebert and Fabre:* Bull. de la Soc. d'Obst. et Gynéc. de Paris **27:** 779, 1928. (11) *Bacon, C. S.:* Am. J. Obst. & Gynec. **23:** 140, 1932. (12) *Ballantyne, J. W.:* Brit. M. J. **2:** 583, 1922. (13) *Barnett, A. M.:* Urol. & Cutan. Rev. **32:** 196, 1928. (14) *Bartholomew, R. A.:* J. A. M. A. **83:** 172, 1924. (15) *Beck, A. C.:* Am. J. Obst. & Gynec. **2:** 416, 1921. (16) *Idem:* N. Y. State J. Med. **26:** 102, 1926. (17) *Belding, David L.:* Am. J. Syph. **9:** 132, 1925. (18) *Idem:* Am. J. Obst. & Gynec. **9:** 203, 1925. (19) *Idem:* Am. J. Syph. **11:** 73, 1927. (20) *Belding, D. L., and Hunter, I. L.:* Am. J. Obst. & Gynec. **8:** 22, 1924. (21) *Bertaccini, G.:* Urol. & Cutan. Rev. **33:** 1, 1929. (22) *Bertin:* Traité de la Maladie vénériénne chez les Enfans nouveau-nés, les Femmes enceintes, et les Nourices, Gabon, Paris, 1810. (23) *Bertin, E.:* Presse med. **34:** 278, 1926. (24) *Bessesen, D. H.:* Med. Times **57:** 109, 1929. (25) *Bigelow, G. H.:* Communicable Disease Control: White House Conference on Child Health and Protection, Century Co., New York and London, 1931. (26) *Bilote, G. H.:* J. A. M. A. **89:** 268, 1927. (27) *Birnbaum, G.:* Deutsche med. Wchnschr. **53:** 1893, 1927. (28) *Bizard, L., and Jolivet, L.:* Presse méd. **33:** 1608, 1925. (29) *Boas, Harald:* Die Prophylaxe der angeborenen Syphilis, Kongenital Syphilis, Handbuch der Haut- und Geschlechtskrankheiten **19:** 327, Julius Springer, Berlin, 1927. (30) *Boas, H., and Gammeltoft, S. A.:* Acta gynec. Scandinav. **1:** 309, 1922. (31) *Boas, H., and Gammeltoft, S. A.:* Arch. f. Gynäk. **128:** 527, 1926. (32) *Boas, H., Gammeltoft, S. A., and Siecke, K.:* Arch. f. Gynäk. **128:** 537, 1926. (33) *Boas, H., and Sodemann, T.:* Arch. f. Dermat. u. Syph. **160:** 183, 1930. (34) *Boas, H., and Sodemann, T.:* Urol. & Cutan. Rev. **34:** 23, 1930. (35) *Bourquin, H.:* Am. J. Physiol. **59:** 122, 1922. (36) *Brown, H., Saleeby, E. R., and Schamberg, J. F.:* J. Pharmacol. & Exper. Therap. **28:** 165, 1926. (37) *Brown, W. H., and Pearce, Louise:* Am. J. Syph. **4:** 593, 1920. (38) *Brown, W. H., and Pearce, Louise:* J. Exper. Med. **39:** 645, 1924. (39) *Browne, F. J.:* Brit. M. J. **2:** 590, 1922. (40) *Idem:* Brit. M. J. **2:** 250, 1927.

(41) *Bruno, Hans:* Dermat. Wchnschr. **83:** 1546, 1926. (42) *Campbell, H. S., and Frost, K.:* Calif. & West. Med. **32:** 231, 1930. (43) *Campos, E. deS.:* Bull. Johns Hopkins Hosp. **34:** 253, 1923. (44) *Carle:* Ann. de Dermat. et Syph. **4:** 451, 1913. (45) *Cathelineau, H.:* Bull. Soc. franç. de Dermat. et Syph. **1:** 167, 1890. (46) *Cathelineau, H., and Stef:* Ann. de Dermat. et Syph. **1:** 972, 1890. (47) *Chesney, A. M.:* J. Exper. Med. **38:** 627, 1923. (48) *Colles, Abraham:* Practical Observations on the Venereal Disease and on the Use of Mercury, A. Waldie, Philadelphia, 1837. (49) *Commiskey, L. J. J.:* Am. J. Obst. **73:** 676, 1916. (50) *Cook, A. R.:* Brit. M. J. **2:** 855, 1929. (51) *Corda, G. M.:* Gior. ital. Dermat. e Sifil. **70:** 945, 1929. (52) *Couvelaire, A., and Mayer, M.:* Bull. de la Soc. d'Obst. et de Gynéc. de Paris **20:** 531, 1931. (53) *Creadick, A. N.:* Am. J. Obst. & Gynec. **2:** 451, 1921. (54) *Cruickshank, J. N.:* Brit. M. J. **2:** 593, 1922. (55) *Idem:* Medical Research Council, Special Report Series, No. 82, London, 1924. (56) *Cunningham:* Am. J. Physiol. **60:** 448, 1922. (57) *d'Aprile, F.:* Clin. Ostet. **27:** 456, 1925. (58) *d'Astros, L., and Teissonnière, M.:* Marseille Méd. **49:** 713, 1912. (59) *de Buys, L. R.:* Am. J. Dis. Child. **5:** 65, 1913. (60) *Dejust, L. H., and Vignes, H.:* Compt. rend. de la Soc. Biol. **93:** 314, 1925. (61) *Diday, P.:* Traité de la Syphilis des Nouveau-nés, Lyon, 1854. Translated by G. Whitley, 1858, William Wood and Co., New York, 1883. (62) *Dodds, G. H.:* J. Obst. & Gynec. Brit. Emp. **34:** 779, 1927. (63) *Duca, A., and Geyer, M.:* Clin. ostet. **33:** 201, 1931. (64) *Dunham, E. C.:* Am. J. Dis. Child. **43:** 317, 1932. (65) *Eastman, N. J.:* Am. J. Obst. & Gynec. **21:** 60, 1931. (66) *Ehrenfest, Hugo:* Am. J. Obst. & Gynec. **21:** 867, 1931. (67) *Emmons, A. B.:* Boston M. & S. J. **162:** 640, 1910. (68) *Esch, P., and Wieloch, J.:* München. med. Wchnschr. **69:** 926, 1922. (69) *Fildes, P.:* J. Obst. & Gynec. Brit. Emp. **27:** 124, 1915. (70) *Fildes, P.:* Lancet **2:** 82, 1915. (71) *Findlay, L.:* Brit. M. J. **2:** 887, 1921. (72) *Idem:* Am. J. Dis. Child. **28:** 133, 1924. (73) *Finger, E., and Landsteiner, K.:* Arch. f. Dermat. u. Syph. **81:** 147, 1906. (74) *Fordyce, J. A.:* Am. J. M. Sc. **149:** 781, 1915. (75) *Fordyce, J. A., and Rosen, I.:* Arch. Dermat. & Syph. **5:** 1, 1922. (76) *Fordyce, J. A., Rosen, I., and Myers, C. N.:* Am. J. Syph. **8:** 65, 1924. (77) *Fournier, A.:* Syphilis and Marriage, G. Masson, Paris, 1880. (78) *Idem:* Leçons clinique sur la Syphilis: Étudiée plus particulièrement chez la Femme, Delahaye et Lecrosnier, Paris, 1881. (79) *Idem:* Semaine méd. **18:** 481, 1898. (80) *Idem:* The Treatment and Prophylaxis of Syphilis, Translated by C. F. Marshall, New York, 1906, Rebman. (81) *Fowler, W. A.:* Am. J. Obst. & Gynec. **9:** 837, 1925. (82) *Fracastor:* Le Mal Francais (Extrait du Livre de Contagionibus, 1546), Translated with notes by Alfred Fournier, Adrien Delahaye, Paris, 1869. (83) *Fraenkel, Ernst:* Arch. f. Gynäk. **5:** 1, 1873. (84) *Funkhouser, W. L., and Dickson, R. W.:* Am. J. Syph. **12:** 542, 1928. (85) *Gammeltoft, S. A.:* Am. J. Obst. & Gynec. **15:** 747, 1928; also in Am. J. Syph. **13:** 194, 1929. (86) *Idem:* Hospitalstidende **74:** 293, 1931. (87) *Gautier, P., and Thevenod, A.:* Nourrisson **17:** 277, 1929. (88) *Gellhorn, G.:* Surg. Gynec. Obst. **32:** 535, 1921. (89) *Gilbert, R., and Langworthy, V.:* Am. J. Syph. **10:** 101, 1926. (90) *Gillespie, J. B.:* Am. J. Dis. Child. **44:** 9, 1932. (91) *Goodman, H.:* Surg. Gynec. Obst. **30:** 368, 1920. (92) *Gougerot, H.:* Paris méd. **43:** 393, 1922. (93) *Idem:* Bull. et mem. de la Soc. méd. des hôp. de Paris **47:** 865, 1923. (94) *Idem:* Presse méd. **38:** 883, 1930. (95) *Idem:* Med. Press & Circ. **133:** 404, 1932. (96) *Greenlees, J. R. C.:* Glasgow M. J. **96:** 270, 1921. (97) *Hall, E. R.:* South. M. J. **18:** 757, 1925. (98) *Halloran, C. R.:* Am. J. Syph. **14:** 222, 1930. (99) *Haskell, R. H.:* J. A. M. A. **64:** 890, 1915. (100) *Haythorn, S. R., and Lacy, G. R.:* J. Infect. Dis. **29:** 386, 1921. (101) *Hemsath, F. A.:* Am. J. Syph. **15:** 396, 1931. (102) *Hendry, R. A.:* Lancet **2:** 986, 1920. (103) *Hinton, W. A.:* Am. J. Syph. **7:** 155, 1923. (104) *Hissard, R.:* Ann. des mal. vén. **26:** 925, 1931. (105) *Hochsinger, K.:* Wien. klin. Wchnschr. **23:** 881 and 932, 1910. (106) *Hoffmann, E.:* Arch. f. Dermat. u. Syph. **160:** 161, 1930. (107) *Holland, E. L., and Lane-Claypon, J. E.:* Child Life Investigation, Med. Research Council **109:** London, 1926. (108) *Jamison, S. C.:* New Orleans M. & S. J. **69:** 96, 1916. (109) *Jeans, P. C.:* Am. J. Dis. Child. **11:** 11, 1916. (110) *Idem:* Am. J. Dis. Child. **20:** 58, 1920. (111) *Jeans, P. C., and Cooke, J. V.:* Am. J. Dis. Child. **22:** 402, 1921. (112) *Jensen-Carlén, K.:* Acta. obst. et Gynec. Scandinav. **8:** 202, 1929. (113) *Jewesbury, R. C.:* Lancet **1:** 962, 1921. (114) *Johnson, G. K.:* Detroit M. J. **1:** 344, 1877. (115) *Jones, S. S.:* Northwest Med. **27:** 526, 1928. (116) *Kassowitz, M.:* New York M. J. **25:** 161, 281, 1877; **26:** 51, 168, 265, 1877; **27:** 254, 601, 1878. (117) *Kerl:* Arch. f. Dermat. u. Syph. **160:** 183, 1930. (118) *Kilduffe, R. A.:* The Clinical Interpretation of the Wassermann Reaction, Philadelphia, 1926, Lea and Febiger. (119) *Kirkpatrick, T. P. C.:* J. State Med. **37:** 153, 1929. (120) *Klaften, E.:* Klin. Wchnschr. **7:** 458, 1928. (121) *Klauder,*

J. V., and Brown, H.: Am. J. Obst. & Gynec. **27:** 60, 1931. (122) *Kolmer, J. A.:* Am. J. Dis. Child. **19:** 344, 1920. (123) *Idem:* Serum Diagnosis by Complement Fixation With Special Reference to Syphilis, Philadelphia, 1928, Lea and Febiger. (124) *Kolmer, J. A., and Schamberg, J. F.:* J. Exper. Med. **15:** 498, 1912. (125) *Kraul, L., and Bodnar, L.:* Arch. f. Gynäk. **128:** 238, 1926. (126) *Kristjansen, Aage:* Hospitalstid., Copenhagen **70:** 97, 1927. Abst. Cong. Syph., U. S. Public Health Service, U. S. Govt. Print. Office, Wash., 1930. (127) *Lakaye, R.:* Arch. méd. Belges **75:** 385, 1922. (128) *Lane, J. L.:* Northwest Med. **27:** 77, 1928. (129) *Lasseur, P., and Vermelin, H.:* Gynéc. et Obst. **7:** 130, 1923. (130) *Laurent, C.:* Urol. & Cutan. Rev. **33:** 242, 1929. (131) *Laurentier, C.:* Bull. soc. franç. dermat. et syph. **39:** 183, 1932. (132) *Lawrence, J. S.:* J. A. M. A. **84:** 432, 1925. (133) *Lee, C. C.:* Am. J. Syph. & Dermat. **2:** 115, 1871. (134) *Lees, D.:* Indian Med. Rec. **47:** 321, 1927. (135) *Lemež, Leo:* Ztschr. f. Kinderh. **48:** 97, 1929. (136) *Leonard, C. S., and Love, R. B.:* J. Pharmacol. & Exper. Therap. **34:** 347, 1928. (137) *Lesné, E., and Linossier-Ardoin, A.:* Le Nourrisson, Paris **21:** 38, 1933. (138) *Lesser, Fritz:* Serologie der kongenitalen Syphilis, Kongenital Syphilis, Handbuch der Haut- und Geschlechtskrankheiten **19:** 287, Julius Springer, Berlin, 1927. (139) *Lombardo, C.:* Giorn. ital. dermat. e sif. **67:** 187, 1926. (140) McCord, J. R.: Am. J. Obst. & Gynec. **11:** 850, 1926. (141) *Idem:* Am. J. Obst. & Gynec. **13:** 100, 1927. (142) *Idem:* Am. J. Obst. & Gynec. **13:** 25, 1927. (143) *Idem:* J. A. M. A. **88:** 626, 1927. (144) *Idem:* South. M. J. **21:** 229, 1928. (145) *Idem:* South. M. J. **23:** 40, 1930. (146) *Idem:* Am. J. Syph. **16:** 78, 1932. (147) *Idem:* Am. J. Syph. **16:** 83, 1932. (148) *Macnicol, M.:* Lancet **2:** 206, 1931. (149) *Mahon, P. A. O., and Lamauvem, L.:* Histoire de la Medécine clinique, et Recherches importantes sur l'Existence, la Nature et la Communication des Maladies syphilitiques dans les Femmes enceintes, etc. Buisson, Gabon, Mequignon, Lenormand, Paris, 1804. (150) *Manouilian, Y.:* Gynéc. et obst. **26:** 10, 1932. (151) *Marcus, K.:* Arch. f. Dermat. u. Syph. **160:** 190, 1930. (152) *Marshall, C. H.:* J. A. M. A. **91:** 102, 1928. (153) *Mauriceau, Francesco:* Trattato delle Malattie delle Donne Gravide e delle Infantate, Libro I, Capitolo XXV, Del Mal Venero della Donna Gravida, p. 141, Luigi Du Four (Cologni), 1685. (154) *Mehlman, I. J.:* Ohio State M. J. **24:** 461, 1928. (155) *Menten, M. L.:* Am. J. Obst. **78:** 514, 1918. (156) *Meyer, E.:* Ztschr. f. Geburtsh. u. Gynäk. **77:** 20, 1915. (157) *Miles, L. M.:* Minnesota Med. **11:** 690, 1928. (158) *Milian, G., and de Douhet:* Rev. franç. de dermat. et vén. **8:** 9, 1932. (159) *Moore, J. E.:* Arch. Int. Med. **30:** 548, 1922. (160) *Idem:* Bull. Johns Hopkins Hosp. **34:** 89, 1923. (161) *Idem:* Ven. Dis. Inf. **11:** 243, 1930; also in J. Med. **12:** 31, 1931. (162) *Morosoff, A. N., and Raskin, M. V.:* Mosk. Med. J. **10:** 42, 1930. (163) *Mossman, H. W.:* Am. J. Anat. **37:** 433, 1926. (164) *Mraček, F.:* Wien. klin. Wehnschr. **16:** 519, 1903. (165) *Nabarro, D.:* Brit. J. Ven. Dis. **4:** 107, 1928. (165a) *Nakayama, J.:* Japanese J. Exper. Med. **11:** 1, 1933. (166) *Nathanson, J. N.:* Surg. Gynec. & Obst. **41:** 320, 1925. (167) *Nicloux, M.:* Obstétrique **14:** 840, 1909. (168) *Pack, G. T., Scharnagel, I., and Veal, J. R.:* Am. J. Syph. **14:** 233, 1930. (169) *Palmer, A. C.:* Med. Research Council, Rpt. 118, London, 1928. (170) *Parker, V. H.:* Med. Woman's J. **34:** 330, 1927. (171) *Parran, T.:* J. A. M. A. **97:** 73, 1931. (172) *Paucot, H., and Nuytten, J.:* J. de méd. de Paris **47:** 939, 1928. (173) *Pendergrass, E. P., and Bromer, R. S.:* Am. J. Roentgen. **22:** 1, 1929. (174) *Pillsbury, D. M.:* Internat. Clin. (41st Series) **2:** June, 1931. (175) *Polak, J. O., and Beres, D.:* Am. J. Surg. **4:** 143, 1928. (176) *Pomaret and Benoit:* Bull. et mem. de la Soc. méd. des hôp. de Paris **47:** 699, 1923. (177) *Pye-Smith, E. J.:* J. Obst. & Gynec. Brit. Emp. **88:** 578, 1931. (178) *Raiziss, G. W.:* J. Pharmacol. & Exper. Therap. **19:** 271, 1922. (179) *Ribadeau-Dumas, L.:* Nourrisson **21:** 175, 1924. (180) *Richter, Wilhelm:* München. med. Wehnschr. **76:** 735, 1929. (181) *Ricord, Philip:* Traité pratique des Maladies Vénériennes, etc. Rouvier et le Bouvier, Paris, 1838. (182) *Rietschel, Hans:* Allgemeine Pathologie der angeborenen Syphilis, Kongenital Syphilis, Handbuch der Haut- und Geschlechtskrankheiten, Julius Springer, Berlin, 1927. (183) *Rittau, M.:* Klin. Wehnschr. **10:** 1539, 1931. (184) *Rivière, M.:* Bull. de la Soc. d'obst. et de gynéc. de Paris **20:** 178, 1931. (185) *Roberts, C. S. L.:* Brit. M. J. **2:** 971, 1923. (186) *Roberts, M. H.:* Am. J. Dis. Child. **45:** 461, 1933. (187) *Rorke:* Lancet **2:** 348, 1923. (188) *Routh, A. J.:* Brit. M. J. **1:** 355 and 720, 1914. (189) *Idem:* Lancet **1:** 45, 1918. (190) *Idem:* Am. J. Syph. **2:** 484, 1918. (191) *Idem:* Lancet **2:** 988, 1920. (192) *Sage, E. C.:* Neb. State M. J. **13:** 405, 1928. (193) *Sandes, G.:* Lancet **2:** 206, 1931. (194) *Sauphar, G.:* Médicine **12:** 306, 1931. (195) *Schamberg, J. F., and Wright, C. S.:* Ven. Dis. Inform. **10:** 421, 1929. (196) *Schauenstein and Spaeth:* Jahrb. der Kinderh. und phys.

Erzieh. **2:** 13, 1859. (197) *Schumann, E. A.:* Am. J. Obst. & Gynec. **8:** 257, 1924. (198) *Schumann, E. A., and Barnes, C. S.:* Am. J. Obst. & Gynec. **2:** 612, 1921. (199) *Schwarz, H.:* Am. J. Dis. Child. **19:** 249, 1920. (200) *Sézary, A.:* Progres méd. p. 956, 1932. (201) *Sharp, O. B.:* J. State Med. **39:** 295, 1931. (202) *Shipley, P. G., Pearson, J. W., Weech, A. A., and Greene, C. H.:* Bull. Johns Hopkins Hosp. **32:** 75, 1921. (203) *Slemons, J. M.:* Am. J. M. Sc. **153:** 212, 1917. (204) *Solomon, H. C., and Solomon, M. H.:* U. S. Interdpt. Soc. Hyg. Board, Wash., 1922. (205) *Solomon, H. C.:* Am. J. Syph. **10:** 96, 1926. (206) *Spencer, H. R.:* History of British Midwifery from 1650 to 1800. John Bale Sons and Danielsson Ltd., London, 1927. (207) *Spiegler, R.:* München. med. Wchnschr. **79:** 95, 1932. (208) *Spitzer, L.:* München. med. Wchnschr. **79:** 97, 1932. (209) *Stacy, W. T.:* Missouri State Med. Assoc. J. **29:** 371, 1932. (210) *Stillians, A. W.:* Arch. Dermat. & Syph. **17:** 318, 1928. (211) *Stokes, John H.:* The Third Great Plague, Philadelphia, 1917, W. B. Saunders Co. (212) *Idem:* Arch. Dermat. & Syph. **4:** 778, 1921. (213) *Idem:* Modern Clinical Syphilology, Philadelphia, 1926, W. B. Saunders Co. (214) *Idem:* Arch. Dermat. & Syph. **22:** 201, 1930. (215) *Strepowski:* Ann. de l'Inst. Pasteur **46:** 52, 1931. (216) *Swediaur, F.:* Traité complete sur les Symptomes, les Effets, la Nature, et le Traitement des Maladies syphilitiques, ed. 4, Paris, 1809. (217) *Thomsen, O., and Boas, H.:* Arch. f. Dermat. u. Syph. **111:** 91, 1912. (218) *Toland, O. J.:* Am. J. Obst. & Gynec. **17:** 411, 1929. (219) *Trinchese, J.:* München. med. Wchnschr. **57:** 570, 1910. (220) *Tüdös, A.:* Jahrb. f. Kinderh. **108:** 236, 1925. (221) *Turnbull, H. M.:* Lancet **1:** 1239, 1922. (222) *Turner, R. H.:* Med. Clin. North America **11:** 1211, 1928. (223) *Turner, T. B.:* Bull. Johns Hopkins Hosp. **46:** 159, 1930. (224) *Uhlenhuth, P., and Mulzer, P.:* Deutsche med. Wchnschr. **39:** 879, 1913. (225) *Underhill, F. P., and Amatruda, F. G.:* J. A. M. A. **81:** 2009, 1923. (226) *Veeder, B. S., and Jeans, P. C.:* Am. J. Dis. Child. **11:** 177, 1916. (227) Ven. Dis. Inform. **6:** 355, 1925. (228) *Voegtlin, C., and Thompson, J. W.:* J. Pharmacol. & Exper. Therap. **20:** 85, 1923. (229) *von Zumbusch, L.:* Die Diagnose der angeborenen Syphilis. Prognose der kongenitalen Syphilis. Handbuch der Haut- und Geschlechtskrankheiten, Berlin, 1927, Julius Springer. (230) *Wallace, W.:* A Treatise on the Venereal Disease and Its Varieties, London, 1833, Burgess and Hill. (231) *Warthin, A. S.:* Am. J. Obst. & Gynec. **15:** 595, 1928. (232) *Wegner, Georg:* Virchow's Arch. f. Path. Anat. u. Physiol. **50:** 305, 1870. (233) *Wells, A. S.:* J. M. A. S. Africa **3:** 331, 1929. (234) *Welz, W. E., and VanNest, A. E.:* Am. J. Obst. & Gynec. **4:** 174, 1922. (235) *Whitehouse, B.:* Brit. M. J. **2:** 1095, 1929. (236) *Wile, U. J.:* Bull. Johns Hopkins Hosp. **51:** 102, 1932. (237) *Wile, U. J., and Shaw, J. W.:* J. A. M. A. **95:** 1791, 1930. (238) *Williams, J. W.:* J. A. M. A. **64:** 95, 1915. (239) *Idem:* Bull. Johns Hopkins Hosp. **31:** 141, 1920. (240) *Idem:* Bull. Johns Hopkins Hosp. **31:** 335, 1920. (241) *Idem:* Bull. Johns Hopkins Hosp. **33:** 383, 1922. (242) *Wilson, Erasmus:* On Syphilis, Constitutional and Hereditary and on Syphilitic Eruptions, Philadelphia, 1852, Blanchard and Lea. (243) *Wingen, T.:* Münch. med. Wchnschr. **73:** 316, 1932. (244) *Woodbury, R. M.:* Infant Mortality and Its Causes, Baltimore, 1926, Williams and Wilkins. (245) World's Health, Paris **6:** 523, 1925. Conference in Paris on Congenital Syphilis. (246) *Young, H. McC.:* Am. J. Syph. **11:** 245, 1927. (247) *Young, W. J.:* Surg. Gynec. & Obst. **30:** 508, 1920. (248) *Zieler, K.:* München. med. Wchnschr. **79:** 663, 1932.

Nuernberger, L.: Proteins of the Vaginal Secretion, Ztschr. f. Geburtsh. u. Gynäk. **102:** 1, 1932.

Sulphydryl (S-H) forms, believed to signify the presence of glutathione, were found both in vaginal secretions and in the vaginal wall. Quantitative determinations of glutathione in the vaginal secretion varied from 28 to 284 mg. per cent. The diamino-acid Arginine was also found in the vaginal secretion.

Grover Liese.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

List of Diplomates (Limiting Practice to Obstetrics and/or Gynecology) Certified to January 1, 1934

ARIZONA

RING, H. H., TUCSON

ARKANSAS

HINKLE, S. B., LITTLE ROCK

CALIFORNIA

ABRAMSON, M. J., LOS ANGELES
AINLEY, F. C., LOS ANGELES
BELL, T. F., OAKLAND
BERNSTEIN, ABRAHAM, SAN FRANCISCO
CRAIG, R. G., SAN FRANCISCO
DE CARLE, D. W., SAN FRANCISCO
EMGE, L. A., SAN FRANCISCO
FALLAS, T. F., LOS ANGELES
FIST, H. S., LOS ANGELES
FLUHMANN, C. F., SAN FRANCISCO
GREENBAUM, G. B., LOS ANGELES
HANLEY, B. J., LOS ANGELES
HOLMES, O. M., SAN MATEO
IRWIN, J. C., LOS ANGELES
JOHNSON, O. D., LOS ANGELES
KRAHULIK, E. J., LOS ANGELES
LAZARD, E. M., LOS ANGELES
LINDENBERG, FRED, LOS ANGELES
LOOMIS, F. M., OAKLAND
LYNCH, F. W., SAN FRANCISCO
MCNEILE, L. G., LOS ANGELES
MAXWELL, ALICE F., SAN FRANCISCO
MOORE, W. G., SAN FRANCISCO
NEWMAN, H. P., SAN DIEGO
PAGE, C. W., BERKELEY
PETTIT, A. V., SAN FRANCISCO
PIERCE, S. N., LOS ANGELES
ROONEY, H. M., LOS ANGELES
ROSS, M. H., LOS ANGELES
SALISBURY, C. S., LOS ANGELES
SHAW, H. N., LOS ANGELES
SHERRICK, J. W., OAKLAND
SHUFELT, A. A., SAN JOSE
SLEMONS, J. M., LOS ANGELES
SPALDING, A. B., SAN FRANCISCO
STEPHENSON, H. A., SAN FRANCISCO
THOMPSON, W. B., LOS ANGELES
TIBER, L. J., LOS ANGELES
TOLLEFSON, D. G., LOS ANGELES
VOLLMER, A. M., SAN FRANCISCO
VRUWINK, JOHN, LOS ANGELES
WILLIAMS, N. H., LOS ANGELES

COLORADO

INGRAHAM, C. B., DENVER
POWELL, CUTHBERT, DENVER
WEINER, MORRIS, DENVER

CONNECTICUT

COGAN, G. E., HARTFORD
CREADICK, A. N., NEW HAVEN
HERSHMAN, A. A., NEW HAVEN
HOWARD, J. H., BRIDGEPORT
LEWIS, R. M., NEW HAVEN
MILLER, J. R., HARTFORD
MORSE, A. H., NEW HAVEN
STORRS, R. W., HARTFORD
THOMPSON, H. G., HARTFORD
THOMS, HERBERT, NEW HAVEN

DISTRICT OF COLUMBIA

DAVIS, DANIEL, WASHINGTON
GARNETT, A. Y. P., WASHINGTON
JACOBS, J. B., WASHINGTON
KANE, H. F., WASHINGTON
MUNDELL, J. J., WASHINGTON
SULLIVAN, R. Y., WASHINGTON
TITUS, E. W., WASHINGTON
WILLSON, PRENTISS, WASHINGTON

GEORGIA

MCCORD, J. R., ATLANTA

ILLINOIS

ADAIR, F. L., CHICAGO
BACON, C. S., CHICAGO
BAER, J. L., CHICAGO
BLOOMFIELD, J. H., CHICAGO
BROWNE, W. H., CHICAGO
BUXBAUM, HENRY, CHICAGO
CAREY, EUGENE, CHICAGO
CORNELL, E. L. CHICAGO
CULBERTSON, CAREY, CHICAGO
CURTIS, A. H., CHICAGO
DANFORTH, W. C., EVANSTON
DELEE, J. B., CHICAGO
DIECKMANN, W. J., CHICAGO
DORLAND, W. A. N., CHICAGO
EDWARDS, E. A., CHICAGO
FALLS, F. H., CHICAGO
FISCHMANN, E. W., CHICAGO
FITZGERALD, J. E., CHICAGO
FOX, P. C., OAK PARK
FRANKENTHAL, L. E., CHICAGO
FRANKENTHAL, L. E., JR., CHICAGO
GALLOWAY, C. E., EVANSTON
GOLDSTINE, M. T., CHICAGO
GOUGH, J. A., CHICAGO
GREENHILL, J. P., CHICAGO
GRIER, R. M., EVANSTON
HEANEY, N. S., CHICAGO
HESSELTINE, H. C., CHICAGO
HOLMES, R. W., CHICAGO
HORNER, D. A., CHICAGO
JONES, H. O., CHICAGO
KANTER, A. E., CHICAGO
LACKNER, J. E., CHICAGO
LASH, A. F., CHICAGO
LITT, SOL, CHICAGO
MAC EACHERN, M. T., CHICAGO
REED, C. B., CHICAGO
RUDOLPH, LOUIS, CHICAGO
SCHMITZ, HENRY, CHICAGO
SCHOCHET, S. S., CHICAGO
SCOTT, R. A., EVANSTON
SERED, HARRY, CHICAGO
SIMON, L. S., CHICAGO
SMITH, P. H., EVANSTON
STEIN, I. F., CHICAGO

INDIANA

BECKMAN, H. F., INDIANAPOLIS
BICKEL, D. A., SOUTH BEND
GUSTAFSON, G. W., INDIANAPOLIS
KELLY, J. F., INDIANAPOLIS
MCCORMICK, C. O., INDIANAPOLIS
MENDENHALL, A. M., INDIANAPOLIS
SMITH, D. L., INDIANAPOLIS
WALKER, F. C., INDIANAPOLIS

IOWA

BROWN, W. E., CEDAR RAPIDS
PLASS, E. D., IOWA CITY
VON GRAFF, ERWIN, IOWA CITY

KANSAS

COWLES, G. E., WICHITA
WEST, R. A., WICHITA

KENTUCKY

MCCONNELL, W. T., LOUISVILLE
SPEIDEL, EDWARD, LOUISVILLE

LOUISIANA

KING, E. L., NEW ORLEANS
KOSTMAYER, H. W., NEW ORLEANS
LEVY, W. E., NEW ORLEANS
MILLER, C. J., NEW ORLEANS
MILLER, H. E., NEW ORLEANS

MAINE

LEIGHTON, A. P., JR., PORTLAND

MARYLAND

BERGLAND, J. McF., BALTIMORE
DOUGLASS, L. H., BALTIMORE
NOVAK, EMIL, BALTIMORE
ROWLAND, J. M. H., BALTIMORE
*WILLIAMS, J. W., BALTIMORE

MASSACHUSETTS

ALMY, THOMAS, FALL RIVER
BRISTOL, D. J., JR., BOSTON
DENORMANDIE, R. L., BOSTON
GOOD, F. L., BOSTON
GOETHALS, T. R., BOSTON
HEFFERNAN, R. J., BOSTON
HUNTINGTON, J. L., BOSTON
IRVING, F. C., BOSTON
JACKSON, D. L., BOSTON
JANNEY, J. C., BOSTON
KELLOGG, F. S., BOSTON
KICKHAM, E. L., BOSTON
LYNCH, F. J., BOSTON
MEAKER, S. R., BOSTON
PAINE, A. K., BOSTON
PEMBERTON, F. A., BOSTON
PHANEUF, L. E., BOSTON
RUGGLES, E. P., BOSTON
RUSHMORE, STEPHAN, BOSTON
SHAY, E. F., FALL RIVER
SMITH, E. W., BOSTON
TITUS, R. S., BOSTON

MICHIGAN

BELL, J. N., DETROIT
CUMMINGS, H. H., ANN ARBOR
KAMPERMAN, GEORGE, DETROIT
MILLER, N. F., ANN ARBOR
PETERSON, REUBEN, ANN ARBOR
SEELEY, W. F., DETROIT
WALSER, H. C., DETROIT
YATES, H. W., DETROIT

MINNESOTA

BARRY, L. W., ST. PAUL
CONDIT, W. H., MINNEAPOLIS
EHRENBERG, C. J., MINNEAPOLIS
LA VAKE, R. T., MINNEAPOLIS
LITZENBERG, J. C., MINNEAPOLIS
MALAND, C. O., MINNEAPOLIS
MANLEY, J. R., DULUTH
MUSSEY, R. D., ROCHESTER
RANDALL, L. M., ROCHESTER
ROTHROCK, J. L., ST. PAUL
SCHULZE, A. G., ST. PAUL
SWANSON, R. E., MINNEAPOLIS

MISSOURI

ASCHMANN, T. H., KANSAS CITY
CALKINS, L. A., KANSAS CITY
CROSSEN, H. S., ST. LOUIS
CROSSEN, R. J., ST. LOUIS
DORSETT, E. L., ST. LOUIS
DRABKIN, CHARLES, ST. LOUIS
EHRENFEST, HUGO, ST. LOUIS
GELLHORN, GEORGE, ST. LOUIS
GUFFEY, D. C., KANSAS CITY
HAMILTON, B. G., KANSAS CITY
HANNA, M. A., KANSAS CITY
JAMES, J. D., SPRINGFIELD
*KERWIN, WILLIAM, ST. LOUIS
KREBS, O. S., ST. LOUIS
MCNALLEY, F. P., ST. LOUIS
NEWELL, Q. U., ST. LOUIS
O'NEILL, J. B., ST. LOUIS
PADDOCK, RICHARD, ST. LOUIS
ROBLEE, M. A., ST. LOUIS
ROYSTON, G. D., ST. LOUIS
SCHWARZ, HENRY, ST. LOUIS
SCHWARZ, O. H., ST. LOUIS
SWAHLEN, P. H., ST. LOUIS
SINGLETON, J. M., KANSAS CITY
TAUSSIG, F. J., ST. LOUIS
VOGT, W. H., ST. LOUIS
WILSON, R. R., KANSAS CITY

NEBRASKA

FINDLEY, PALMER, OMAHA
LUIKART, RALPH, OMAHA
SAGE, E. C., OMAHA

NEW JERSEY

CONOWAY, W. P., ATLANTIC CITY
COSGROVE, S. A., JERSEY CITY
DARNALL, W. E., ATLANTIC CITY
HALL, P. O., JERSEY CITY
ILL, E. J., NEWARK
MAC KENZIE, R. A., ASBURY PARK
MOUNT, W. B., MONTCLAIR
PUDNEY, W. K., MONTCLAIR
WALKER, R. B., NEW BRUNSWICK

NEW YORK

ABBENE, M. L., BROOKLYN
ACKEN, H. S., JR., BROOKLYN
ADLER, N. H., BROOKLYN
ARANOW, HARRY, NEW YORK
AYRES, D. R., NEW YORK
AYERS, H. E., NEW YORK
BECK, A. C., BROOKLYN
BISHOP, ELIOT, BROOKLYN
BONNER, ADOLPH, BROOKLYN
BRANDT, M. L., NEW YORK
BRETTAUER, JOSEPH, NEW YORK
BRODER, N. E., NEW YORK
BRODHEAD, G. L., NEW YORK
CALDWELL, W. E., NEW YORK
CHERRY, T. H., NEW YORK
CLIFFORD, J. S., ROCHESTER
COHEN, MOSES, LONG ISLAND CITY
CORSCADEN, J. A., NEW YORK
COWLES, H. C., NEW YORK
DANNREUTHER, W. T., NEW YORK
DAVIS, G. H., BROOKLYN
DENNEN, E. H., NEW YORK
DICKINSON, R. L., NEW YORK
DOYLE, F. B., BROOKLYN
FALK, H. C., NEW YORK
FARRAR, LILIAN K. P., NEW YORK
FLINT, AUSTIN, NEW YORK
FRANK, R. T., NEW YORK
FREED, F. C., NEW YORK
FULKERSON, L. L., NEW YORK
FURNISS, H. D., NEW YORK
GAMBLE, T. O., ALBANY
GEIST, S. H., NEW YORK
*GIBSON, GORDON, BROOKLYN
GODSICK, W. H., NEW YORK
GOFF, B. H., NEW YORK
GOLDBERGER, M. A., NEW YORK
GOLDSBOROUGH, F. C., BUFFALO
GORDON, C. A., BROOKLYN
GRAD, HERMAN, NEW YORK
GREENBERG, SARAH K., BROOKLYN
HAGSTROM, H. T., BROOKLYN
HALE, WILLIAM, JR., UTICA
HALSTED, HARBECK, NEW YORK
*HARPER, P. T., ALBANY
HARRAR, J. A., NEW YORK
HEALY, W. P., NEW YORK
HELLMAN, A. M., NEW YORK
HILDRETH, WARREN, NEW YORK
HOENIG, EDWARD, NEW YORK
HOLDEN, F. C., NEW YORK
HOLLADAY, E. W., NEW YORK
HORNSTEIN, MARK, NEW YORK
HOROWITZ, E. A., NEW YORK
HUMPSTONE, O. P., BROOKLYN
HYAMS, M. N., NEW YORK
HYDE, C. R., BROOKLYN
JACOBY, ADOLPH, NEW YORK
JARCHO, JULIUS, NEW YORK
JELLINGHAUS, C. F., NEW YORK
JEWETT, W. A., BROOKLYN
JUDD, A. M., NEW YORK

*Deceased

KAHN, I. W., NEW YORK
KAHN, M. E., BUFFALO
KING, J. E., BUFFALO
KNIPE, W. H. W., NEW YORK
KOSMAK, G. W., NEW YORK
LILIENFELD, M. C. C., NEW YORK
LOBSENZ, MOSES, NEW YORK
LOIZEAUX, L. S., NEW YORK
LUBIN, SAMUEL, BROOKLYN
LYON, E. C., JR., NEW YORK
MCMAHON, J. J., NEW YORK
MCPHERSON, ROSS, NEW YORK
MATTHEWS, H. B., BROOKLYN
MAYES, H. W., BROOKLYN
MENCKEN, H. P., ASTORIA, L. I.
MILLER, J. A., NEW YORK
MOENCH, G. L., NEW YORK
MURRAY, P. M., NEW YORK
NEUSTAEDTER, THEODORE, NEW YORK
PEIGHTAL, T. C., NEW YORK
PHILIP, ALBERT, NEW YORK
*POLAK, J. O., BROOKLYN
POTTER, I. W., BUFFALO
POTTER, M. G., BUFFALO
QUIGLEY, J. A., ROCHESTER
RABBINER, BENJAMIN, BROOKLYN
RAWLS, R. M., NEW YORK
RICE, F. W., NEW YORK
RITCHIE, R. N., ROCHESTER
ROBINSON, M. R., NEW YORK
RONGY, A. J., NEW YORK
ROSENFELD, S. S., NEW YORK
RUBIN, I. C., NEW YORK
RYDER, G. H., NEW YORK
SAFFORD, H. B., NEW YORK
SCHNEIDER, MAX, NEW YORK
SCHOENECK, HENRY, SYRACUSE
SCHWARTZ, L. S., BROOKLYN
SEARS, N. P., SYRACUSE
SIEGEL, L. A., BUFFALO
SMITH, F. R., NEW YORK
SMITH, W. S., BROOKLYN
STANDER, H. J., NEW YORK
STEIN, ARTHUR, NEW YORK
STURMDORF, ARNOLD, NEW YORK
TAYLOR, H. C., NEW YORK
TRUEX, S. L., MIDDLETOWN
VAN AUKEN, W. B. D., TROY
VAN ETTEN, R. C., NEW YORK
WARD, G. G., NEW YORK
WARD, WILBUR, NEW YORK
WATSON, B. P., NEW YORK
WELTON, T. S., BROOKLYN
WILENS, IRA, NEW YORK
WILLIAMSON, H. C., NEW YORK
WILSON, K. M., ROCHESTER
WING, L. A., NEW YORK
WINKLER, E. G., BUFFALO
WOLFE, S. A., BROOKLYN

NORTH CAROLINA

PROCTOR, L. M., RALEIGH
LEE, T. L., KINSTON
ROSS, R. A., DURHAM

NORTH DAKOTA

FJELDE, J. H., FARGO
MOORE, J. H., GRAND FORKS

OHIO

BILL, A. H., CLEVELAND
*BONIFIELD, C. L., CINCINNATI
DOUGLASS, M. D., CLEVELAND
FULLERTON, W. D., CLEVELAND
GARDINER, J. P., TOLEDO
GOODMAN, S. J., COLUMBUS
HOERNER, J. K., DAYTON
KRIGBAUM, R. E., COLUMBUS
MCCLENAHAN, H. E., YOUNGSTOWN
MILLER, THEODORE, CLEVELAND
PIERCE, J. M., CINCINNATI
REYCRAFT, J. L., CLEVELAND
ROGERS, ANDREWS, COLUMBUS
TATE, M. A., CINCINNATI
WEIR, W. H., CLEVELAND

*Deceased

OKLAHOMA

CHARBONNET, P. N., TULSA

OREGON

ADAMS, T. W., PORTLAND
MATHIEU, ALBERT, PORTLAND
*MCCUSKER, C. J., PORTLAND
SCHAUFFLER, G. C., PORTLAND
WATKINS, R. E., PORTLAND

PENNSYLVANIA

ANSPACH, B. M., PHILADELPHIA
BARNARD, E. P., PHILADELPHIA
BEHNEY, C. A., PHILADELPHIA
BLAND, P. B., PHILADELPHIA
CARROLL, T. B., PITTSBURGH
CHALFANT, S. A., PITTSBURGH
CLEMMER, LEON, PHILADELPHIA
CRAIG, E. B., PHILADELPHIA
ELY, W. C., PHILADELPHIA
FISHER, J. M., PHILADELPHIA
FOULKROD, COLLIN, PHILADELPHIA
GILLIS, R. A. D., PITTSBURGH
HAMMOND, F. C., PHILADELPHIA
JAMES, D. B., PHILADELPHIA
JAMES, J. E., JR., PHILADELPHIA
KATZ, DAVID, PITTSBURGH
KEENE, F. E., PHILADELPHIA
KIMBROUGH, R. A., JR., PHILADELPHIA
KOCYAN, J. J., WILKES BARRE
LONGAKER, DANIEL, PHILADELPHIA
*MCCULLOUGH, F. J., PHILADELPHIA
MACFARLANE, CATHARINE, PHILADELPHIA
MANN, BERNARD, PHILADELPHIA
MAZER, CHARLES, PHILADELPHIA
MENGERT, W. F., PHILADELPHIA
NICHOLSON, W. R., PHILADELPHIA
NORRIS, C. C., PHILADELPHIA
PARKE, W. E., PHILADELPHIA
PIPER, E. B., PHILADELPHIA
RAYMOND, W. C., JOHNSTOWN
REEVES, T. K., PITTSBURGH
SCHUMANN, E. A., PHILADELPHIA
STEVENSON, J. W., PITTSBURGH
STURGIS, MARGARET C., PHILADELPHIA
TAYLOR, J. S., ALTOONA
TITUS, PAUL, PITTSBURGH
TRACY, S. E., PHILADELPHIA
VAUX, N. W., PHILADELPHIA
WILLIAMS, P. E., PHILADELPHIA

RHODE ISLAND

APPLETON, PAUL, PROVIDENCE
HALE, F. S., PROVIDENCE

SOUTH CAROLINA

WILSON, L. A., CHARLESTON

TENNESSEE

BLACK, W. T., MEMPHIS
BURCH, L. E., NASHVILLE
PRIDE, W. T., MEMPHIS
REINBERGER, J. R., MEMPHIS
SCHREIER, P. C., MEMPHIS
*TOOMBS, P. W., MEMPHIS

TEXAS

BOURLAND, J. W., DALLAS
COOKE, W. R., GALVESTON
GROGAN, R. L., FORT WORTH
HANNAH, C. R., DALLAS
MAXWELL, W. W., SAN ANTONIO
PASSMORE, B. H., SAN ANTONIO
ROBINSON, H. R., GALVESTON

VERMONT

EASTMAN, O. N., BURLINGTON

VIRGINIA

ANDREWS, C. J., NORFOLK
BAUGHMAN, GREER, RICHMOND
GRAY, B. H., RICHMOND
RUCKER, M. P., RICHMOND

*Deceased

WASHINGTON
BELL, W. W., SEATTLE
THOMPSON, G. G., SEATTLE

WEST VIRGINIA
BLOSS, J. R., HUNTINGTON

WISCONSIN
CAMPBELL, R. E., MADISON
DAVIS, C. H., MILWAUKEE
HARRIS, J. W., MADISON

CANADA
*CLELAND, F. A., TORONTO
HENDRY, W. B., TORONTO
LITTLE, H. M., MONTREAL
SCOTT, W. A., TORONTO
SHUTE, E. V., LONDON
VAN WYCK, H. B., TORONTO

SYRIA
DORMAN, H. G., BEIRUT

*Deceased

Riff: Trichomonas Vaginalis, A Pathogenic Agent, Bull. de la Soc D'obst. et de Gynéc. **4**: 308, 1932.

It is the belief of Riff that when women complain of pruritus around the external genital organs, the responsible cause in nine cases out of ten is the Trichomonas vaginalis. In the tenth case other organisms such as the oidium albicans are the source of the discomfort. He is also of the opinion that Trichomonas vaginalis vaginitis is transmitted from one woman to another when, e. g., sharing the same bed, the same towels, wash basins, wash cloths, bath water or toilet seats. The Trichomonas vaginalis is readily destroyed by many disinfectants but recurrences are frequent. To obtain a cure it is necessary to expose the vaginal mucosa with a speculum, smooth out all folds and apply the solution to all parts of the vagina. Silver nitrate (2 per cent) is excellent as also are bichloride of mercury douches, followed by tampons saturated with borax and glycerine. The author obtained excellent results by means of daily vaginal douches for a period of 21 days.

J. P. GREENHILL.

Goodall, James R.: A Simple and Effective Treatment for Infection With Trichomonas Vaginalis, Canadian M. A. J. **25**: 292, 1931.

Trichomoniasis is caused by the Trichomonas vaginalis, which probably "originates" from the bowel. The disease is not transmissible to the husband and is not infrequently mistaken for gonorrhea. It is readily diagnosed by the hanging drop method in both acute and chronic states.

The treatment of the author's twenty-two cases consisted of using 1 per cent picric acid in vaginal cones applied daily and supplemented with plain water, soap solution, or lactic acid douches. These cases were cured in from eight to ten days. Prophylactically, cones may be used after menstrual periods, which he explains gave such good results that he had only two recurrences. This therapy is also applicable during pregnancy.

H. CLOSE HESSELTINE.